EXHIBIT F

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 2895
DeGRADO *et al.*	Art Unit: 1617
Appl. No. 10/801,951 (Appeal No. 2010-005832) Filed: March 17, 2004	Examiner: Chong, Yong Soo
For: **Facially Amphiphilic Polymers and Oligomers and Uses Thereof**	Atty. Docket: 1694.0630003/JMC/M-R

Declaration of Richard W. Scott, Ph.D. Under 37 C.F.R. § 1.132

Board of Patent Appeals and Interferences
US Patent and Trademark Office
PO Box 1450
Alexandria, Virginia 22313-1450

Dear Sirs:

I, the undersigned, Dr. Richard W. Scott, residing at 961 Wes Moore Drive, West Chester, PA 19382 declare and state as follows based on my personal knowledge:

I. My Background

1. I have a Ph.D. in Microbiology from the University of Pennsylvania. Between 1985 and 1990, I was a Principal Investigator for E. I. DuPont deNemours. From 1991-2001, I worked for Cephalon, Inc., first as a Senior Scientist, then as a Director, Senior Director, and, finally, Vice President. I was Director, Center for Technology Transfer at the University of Pennsylvania between November 2001 and November 2002. Since December 2002, I have been Vice President of Research at PolyMedix, Inc. ("PolyMedix"). A copy of my curriculum vitae is attached as Exhibit 1.

2. As Vice President of Research, I oversee the scientists who identify lead compounds for further development. (Exhibit 1, page 1.) Some of these compounds are synthetic, small, antimicrobial molecules containing a repeating subunit of two aromatic rings linked by a

peptide bond . Other compounds currently being tested are amphiphilic molecules containing two aromatic rings linked by a peptide bond. All of these compounds are classified as defensin-mimetic compounds.

3. The research teams identified and selected two lead compounds that have successfully completed human Phase 1 clinical trials and are currently in Phase 2 clinical trials. (*Id.*) One compound in Phase 2 clinical trials is a defensin-mimetic compound that has shown activity against staphylococcal agents. (*Id.*) Therefore, as expected and designed, this compound exhibits antimicrobial activity. The antimicrobial compound in Phase 2 clinical trials is a synthetic, amphiphilic, small molecule containing a peptide bond connecting two aromatic rings.

II. PolyMedix

4. PolyMedix was founded in 2002, by Nicholas Landekic, William DeGrado, and myself. For the past nine (9) years, PolyMedix has worked to develop lead compounds using pioneering, proprietary computational drug design technology invented by Drs. William DeGrado and Michael Klein. (Exhibit 2.) Drs. DeGrado and Klein, as well as others, developed this technology while at the University of Pennsylvania. (*Id.*)

5. PolyMedix has exclusively licensed technology from the Trustees of the University of Pennsylvania. This exclusive license includes patents and pending applications to the patents and pending patent applications directed to compounds identified using the pioneering, proprietary computational drug design technology and the uses of these compounds, including the application that is the subject of this appeal.

6. A video of Nicholas Landekic, co-founder, President, Chief Executive Officer, and Director of PolyMedix, is available at http://www.polymedix.com/ (last accessed June 16, 2011). In the video, Mr. Landekic describes the founding, research, funding, and intellectual property of PolyMedix, including the compounds PolyMedix currently has in clinical trials.

7. PolyMedix is involved in important research to identify and develop effective treatments of microbial infections. As evidence of the importance of PolyMedix's research efforts, it has received multiple grants to develop antimicrobial and anti-heparin oligomers that fall within one or more claims originally filed in the above-captioned application. For example, PolyMedix has received grants and research contracts from the National Institutes of Health ("NIH"), Defense Threat Reduction Agency ("DTRA"), Office of Naval Research, U.S. Army Research Office, and U.S. Government's Qualifying Therapeutic Discovery Project ("QTDP"). (Exhibits 3-8.) Examples of recent grants and contracts PolyMedix has received are as follows.

a. PolyMedix and the University of Massachusetts - Amherst received a $750,000 Phase 2 Small Business Technology Transfer ("STTR") contract from the U.S. Army Research Office to conduct further testing on antimicrobial compounds. (Exhibit 3.)

b. PolyMedix was awarded two cash grants totaling $488,958 under QTDP to develop (i) PMX-30063, a novel defensin-mimetic antibiotic compound that is in a Phase 2 clinical trial as an initial treatment for Acute Bacterial Skin and Skin Structure Infections caused by *Staph* and (ii) PMX-60056, a synthetic small-molecule anticoagulant reversing agent. (Exhibit 4.)

c. PolyMedix received a $986,000 Phase 2 grant from the NIH to support the development of defensin mimetic antimicrobial compounds for the treatment of oral candidiasis. (Exhibit 5.)

d. PolyMedix and the University of Massachusetts – Amherst received a grant from the Cooperative Research Partnerships for Biodefense and Emerging Infectious Disease of the NIH to develop antimicrobial defensin-mimetic compounds for biodefense and food-borne infectious diseases. The potential value of the grant is up to a total of $6.6 million over a five year period. (Exhibit 6.)

e. PolyMedix and the University of Massachusetts received a Phase I STTR sponsored by the Office of Naval Research in an amount up to $99,838 to identify lead antimicrobial compounds against bacteria that are the most relevant to the military. (Exhibit 7.)

f. PolyMedix received a $1.6 million research contract from DTRA to develop new defensin-mimetic antibiotic compounds to combat biowarfare pathogens. (Exhibit 8.)

III. Pioneering, Proprietary Computer Modeling Technology

8. Langreth, R., "Antibiotic Artisan," *Forbes*, 187:42-44 (February 14, 2011) ("the *Forbes* article") profiled Dr. DeGrado and the computational computer modeling technology he developed with Dr. Klein that PolyMedix has utilized in developing antimicrobial compounds. A copy of the Forbes article is provided as Exhibit 9.

a. According to the *Forbes* article, while biotech companies generally create new drugs by making only small changes to natural proteins, this is not the path Drs. DeGrado and Klein took. Specifically, the *Forbes* article discloses that "[t]he biotech industry creates new drugs by making tweaks to natural proteins. University of Pennsylvania chemist William DeGrado is more of an artist than a tweaker. He has spent much of this career designing new proteins from scratch . . . ." (Exhibit 9, p. 42.)

b. The *Forbes* article also discloses that "DeGrado, with the help of a powerful supercomputer simulation, has created new antibiotics that mimic natural ones but are far simpler to produce and more stable." (*Id.*, p. 44.)

c. Further, the *Forbes* article states that "[t]he first antibiotic from this work is now in human trials at the biotech firm PolyMedix, which DeGrado cofounded in 2002. In animal tests PolyMedix's drug PMX-30063 is at least as powerful as the gold standard hospital antibiotic vancomycin at killing key strains." (*Id.*)

d. The defensin mimetic antimicrobial compounds are new and unlike any previous antimicrobial drug compounds. Drs. DeGrado and Klein developed a pioneering, proprietary computational technology to aid in the design of these compounds.

9. The specification of the above-captioned application describes computer-aided computational techniques able to select potential antimicrobial oligomers. (Specification, pp. 108-112, paras. [0269]-[0277].)

a. According to the specification of the above-captioned application, "[t]he polymers and oligomers of the present invention are designed using computer-aided computational techniques, such as *de novo* design techniques, to embody the amphiphilic properties believed to be important for activity." (*Id.*, p. 108, para. [0269].) Specifically, according to the specification,

> In general, *de novo* design of oligomers is done by defining a three-dimensional framework of the backbone assembled from a repeating sequence of monomers using molecular dynamics and quantum force field calculations. Next, side groups are computationally grafted onto the backbone to maximize diversity and maintain drug-like properties. The best combinations of functional groups are then computationally selected to produce a cationic, amphiphilic structures. Representative compounds are synthesized from this selected library to verify structures and test their biological activity.

(*Id.*, pp. 108-09, para. [0269].)

b. The currently pending application discloses that in one embodiment, the computation technique used to identify polymer backbones that can produce facially amphiphilic polymers and oligomers involves:

> (1) selecting a [sic] polymer backbones or scaffolds suitable for regiospecific introduction of polar (P) and nonpolar (NP) groups;
> (2) determining parameters for a molecular mechanics force field utilizing *ab initio* quantum mechanical calculations;
> (3) calculating energetically accessible conformations of the backbone using molecular dynamics or molecular mechanics calculations;
> (4) identifying energetically accessible conformations of the backbone wherein the periodicity of a geometrical/conformational repeat matches a sequence repeat;
> (5) synthesizing monomers with polar and nonpolar substituents; [and]
> (6) synthesizing an antimicrobial polymer containing the monomers by solution or solid-phase synthesis.

(*Id.*, p. 112, para. [0277].)

10. The specification of the above-filed application indicates that Tew, G.N., *et al.*, "*De novo* design of biomimetic antimicrobial polymers," *PNAS*, 99: 5110-5114 (2002) ("the Tew paper") discloses arylamide polymers designed using *de novo* computational design techniques. (Specification, p. 9, [0021].) A copy of the Tew paper is provided as Exhibit 10.

a. The Tew paper lists Gregory N. Tew, Dahui Liu, Bin Chen, Robert J. Doerksen, Justin Kaplan, Patrick J. Carroll, Michael L. Klein, and William F. DeGrado as authors and describes the computational techniques Drs. DeGrado, Klein, and Tew used to design amphiphilic polymers and oligomers exhibiting antimicrobial activity. (Exhibit 10, p. 5111.)

b. According to the Tew paper, "[c]ritical to the design of folded polymers is the development of accurate computational methods, analogous to those developed for peptide and protein structures that can predict low-energy conformations of the backbone." (*Id.*)

c. Therefore, the Tew paper discloses that the pioneering computational techniques developed by Drs. DeGrado, Klein, Tew, and others were utilized to design new oligomers having a common structure and activity.

IV. The '102 Patent

11. On March 7, 2002, PCT application No. PCT/US02/22043 ("the '043 PCT application"), listing William F. DeGrado, Gregory N. Tew, Michael L. Klein, Dahui Liu, and Jing Yuan as inventors, was filed, claiming the benefit of U.S. Provisional Application No. 60/274,145, filed March 8, 2001. U.S. application No. 10/471,028 ("the '028 application") is a national stage entry application of the '043 PCT application. The '028 application issued as U.S. Patent No. 7,173,102 ("the '102 patent"). A copy of the '102 patent is attached as Exhibit 11.

a. The '102 patent is the first U.S. patent with claims directed to facially amphiphilic polymers designed using the pioneering, proprietary computational drug design technology of Drs. DeGrado, Klein, Tew, and others discussed in Section III above.

b. Specifically, the claims of the '102 patent are directed to facially amphiphilic polymers and their uses in microbiocidal compositions that are to be applied to surfaces of a substrate, such as plastic, wood, or cloth. (Exhibit 11, col. 33, line 1 to col. 46, line 56.)

c. For example, claim 1 of the '102 patent is directed to a genus of polymers or oligomers that encompass polyarylamides substituted with polar and nonpolar groups. (Exhibit

11, col. 33, line 1 to col. 34, line 14.) The substituted polyarylamides of the '102 patent can contain repeating subunits of two aromatic rings linked by a peptide bond. These polymers and oligomers can contain 2 to about 500 polyarylamide subunits. Therefore, the polymers and oligomers of claim 1 of the '102 patent contain 4 to about 1000 aromatic rings each linked by an amide bond.

d. Additionally, claims 26 and 27 of the '102 patent are directed to a method of killing microorganisms comprising providing a substrate (claim 26) that is selected from the group consisting of wood, synthetic polymers, plastics, natural and synthetic fibers, cloth, paper, rubber and glass (claim 27) having disposed thereof a contact killing, facially amphiphilic polymer or oligomer of claims 1, 14, or 20, and placing the facially amphiphilic polymer or oligomer on the substrate in contact with a microorganism to allow formation of pores in the cell wall of the microorganism. (Exhibit 11, col. 45, lines 14-36.) Therefore, the claims of the '102 patent are directed to a method of applying a polymer or oligomer containing up to about 1000 aromatic rings linked by an amide bond to a substrate, such as wood, a synthetic polymer, a plastic, a natural or synthetic fiber, cloth, paper, rubber, or glass.

V. The '951 Application

12. The above-captioned application, U.S. Application No. 10/801,951 ("the '951 application"), was filed March 17, 2004, claiming the benefit of U.S. Provisional Application Nos. 60/455,479, filed March 17, 2003; 60/530,630, filed December 19, 2003; and 60/536,980, filed January 20, 2004. The '951 application lists William F. DeGrado, Dahui Liu, Gregory N. Tew, Michael L. Klein, Jing Yuan, and Sungwook Choi as inventors.

a. The subject matter of the '951 application is a further application of the pioneering computational drug design technology of Drs. DeGrado, Klein, Tew, and others discussed in Section III above.

b. The inventors of the '951 application discovered that shorter amphiphilic oligomers are effective when utilized in a pharmaceutical composition administered to an animal to treat a microbial infection in the animal, a different use than that claimed by the '102 patent. Specifically, the '951 application is directed to "methods of use of facially amphiphilic polymers and oligomers, including pharmaceutical uses of the polymers and oligomers as antimicrobial agents and antidotes for hemorrhagic complications associated with heparin therapy." (Specification, p. 1, para. [0002].)

c. The '951 application discloses that naturally occurring host defense peptides with bactericidal, antifungal, and antiviral activity, although composed of many different amino acid sequences, possess similar physicochemical properties, specifically facial amphiphilicity. (Specification, pp. 2-6, para. [0004]-[0013].) Specifically, the '951 application states, "facial amphiphilicity, *i.e.*, the alignment of polar (hydrophilic) and nonpolar (hydrophobic) side chains on opposite faces of a secondary structural element formed by the peptide backbone, and not amino acid sequence or any particular secondary/tertiary structure, chirality or receptor specificity, is responsible for the biological activity of these peptides." (Specification, p. 6, para. [0013].) Therefore, naturally occurring antimicrobial peptides have a common secondary and tertiary structure consisting of polar and nonpolar groups - amphiphilicity.

d. The '951 application discloses that the oligomers of the invention, including the oligomers of claims 16-48 of the '951 application, were designed to mimic the amphiphilic structure of the naturally occurring antimicrobial peptides. Specifically, according to the '951

application, "these compounds mimic the structure and biological activity of host defense peptides . . . ." (Specification, p. 15, para. [0059].) "The polymers and oligomers of the present invention are capable of adopting amphiphilic conformations that allow for the segregation of polar and nonpolar regions of the molecule into different spatial regions and provide the basis for a number of uses." (Specification, p. 16, para. [0062].) Therefore, the '951 application discloses that the oligomers were designed based upon the common secondary and tertiary structure consisting of polar and nonpolar groups of the naturally occurring antimicrobial peptides – an amphiphilic structure.

e. The '951 specification also discloses that it is the amphiphilic structure of the oligomers of the invention that is responsible for the antimicrobial activity of the oligomers of the invention, including the oligomers of claims 16-48. Specifically, the '951 specification discloses that "polymers and oligomers of the invention adopt amphiphilic conformations that are capable of disrupting the integrity of the cell membrane of microorganisms, resulting in the inhibition of growth or the death of the microorganisms. As a consequence, the polymers and oligomers have a broad range of antimicrobial activity and are effective against a variety of microorganisms, including gram-positive and gram-negative bacterial, fungi, yeast, mycoplasmas, mycobacteria, protozoa, and the like." (Specification, p. 16, para. [0062].) Therefore, the '951 specification discloses that the common amphiphilic structure of the oligomers of the invention is responsible for their exhibited antimicrobial activity.

f. The '951 specification further discloses that these synthetic amphiphilic oligomers are cheaper to prepare and are safer than the naturally occurring peptides. Specifically, the '951 specification indicates that the "non-peptidic mimetics are significantly smaller and easier to prepare than their naturally occurring counterparts . . . are significantly less toxic towards

human erythrocytes, much less expensive to prepare, and are expected to be much more stable *in vivo*." (Specification, p. 15, para. [0059].)

g. The '951 specification discloses that in addition to the common amphiphilic structure of the oligomers of the invention, the oligomers also have a common core structure. This common core structure constitutes aromatic or aliphatic monomers, such as an aromatic ring, linked by an amide or an ester bond. (Specification, pp. 17-18, para. [0067].)

h. Furthermore, the '951 specification discloses that because the synthetic amphiphilic oligomers mimic the structure of naturally occurring peptides, bacterial resistant strains are unlikely to occur. (Specification, p. 15, para. [0059] ("[B]ecause these compounds mimic the structure and biological activity of host defense peptides, the appearance of bacterial resistant strains is very unlikely to occur.").)

i. Therefore, the '951 specification discloses that the inventors designed antimicrobial oligomers containing a peptide bond linking two aromatic rings and that also are amphiphilic – having a hydrophobic face and a hydrophilic face.

13. PolyMedix has conducted *in vitro* and *in vivo* studies utilizing amphiphilic oligomers containing a peptide bond linking two aromatic rings. The results from these studies confirm that oligomers having this common peptide-aromatic core and that also have an amphiphilic structure exhibit antimicrobial activity.

14. In fact, the claims as originally filed in the '951 application encompass oligomers currently in Phase 2 clinical trials sponsored by PolyMedix. Furthermore, the claims as originally filed encompass a genus of oligomers that is the subject of further research and development by PolyMedix.

IV. The Principle Inventors of the '102 Patent and the '951 Application

15. Dr. William DeGrado, a co-founder and member of PolyMedix's Scientific Advisory Board, is Raizus Professor of Biochemistry and Biophysics at the Medical School of the University of Pennsylvania. (Exhibits 2, 9, 12, & 13.) Dr. DeGrado is also an adjunct member of the Chemistry Department at the University of Pennsylvania. (Exhibits 12 & 13.) Dr. DeGrado is a member of the National Academy of Sciences and the American Academy of Arts and Sciences. (Exhibits 2, 12, & 13.) Additionally, Dr. DeGrado has earned the Merryfield and Hirschman Chemistry Awards. (Exhibits 2 & 13.) Dr. DeGrado has published more than 250 papers and has many patents. (Exhibits 2, 12, & 13.)

16. Dr. Michael Klein, also a member of PolyMedix's Scientific Advisory Board, was Director of the Laboratory for Research on the Structure of Matter at the University of Pennsylvania before he retired from the University of Pennsylvania in 2009. (Exhibits 2 & 14.) Dr. Klein became the director of the new Institute for Computation Molecular Science at Temple University. (Exhibits 9 & 14.) Dr. Klein is a member of the National Academy of Sciences, the Royal Society, and the American Academy of Arts and Sciences, and he has published more than 500 papers. (Exhibits 2 & 14.)

17. Dr. Gregory N. Tew, a member of PolyMedix's Scientific Advisory Board, is currently an Associate Professor in the Polymer Science and Engineering Department at the University of Massachusetts – Amherst. (Exhibits 2 & 15.) He was a post-doctoral fellow in Dr. DeGrado's laboratory between 2000 and 2001. (Exhibits 9 & 15.) Dr. Tew has published more than 100 papers and has received several prestigious scientific awards, including the PECASE award for Scientists and Engineers, one of the highest honors given by the U.S. federal government for young scientists. (Exhibits 12 & 15.)

VI. University Developed Inventions

18. As indicated on my curriculum vitae, I was the Director of the Center for Technology Transfer at the University of Pennsylvania. (Exhibit 1.)

a. In my experience, inventors affiliated with universities often develop and patent cutting-edge technologies with broad application. Universities do not have the resources to commercially develop the cutting-edge, platform technologies. Instead, the universities would license these patents to companies which invest the time and money required to commercially develop the patented technology.

b. This is exactly what occurred regarding this pioneering invention. In the present instance, PolyMedix was formed to commercialize the discoveries and inventions of Drs. DeGrado, Klein, Tew, and their associates.

VII. Value of Intellectual Property to Small Biotech Companies

19. A broad intellectual property (IP) foundation is critically important for investor interest in start-up and young biotechnology companies.

a. In the early years of a company's lifetime, the path of product development is often unpredictable, especially with a ground-breaking, platform technology where many applications are possible. Therefore, investors seek protection over a wide range of potential products and product applications to permit development along the most productive avenues which are often not known until years later. Investors thus invest in the prospect of future drugs as evidenced by the strength of the intellectual property.

b. A broad IP basis is also important to protect a company's developing product line from look-alike products that share the overall design principles but differ in specific, possibly insignificant, features. Without this level of protection, investors are wary to participate from fear in losing their investment to follow-on companies that have exploited the other company's groundbreaking technology by finding holes in its intellectual property.

c. In short, without breadth and depth of intellectual property protection, it is impossible to obtain financing for a start-up biotechnology company, and the development of many desperately needed medicines would not occur.

d. PolyMedix is a small, start-up company, developing a pioneering platform technology. Therefore, the scope of its intellectual property is an important consideration for investors and thus is a vital property asset.

20. PolyMedix is currently investigating a large number of compounds for antimicrobial, antiviral, antifungal, and anti-heparin activity and is still in the early stages of identifying and developing additional active compounds. Because of the time and expense required to investigate, identify and develop lead compounds, PolyMedix needs assurance that it has broad patent protection. If PolyMedix had to investigate compounds within a narrow claim scope, PolyMedix would be limited in as to which compounds were tested. As such, some compounds that PolyMedix may eventually find to be the most effective may never have been developed if PolyMedix was unable to pursue and acquire broad patent protection.

21. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the present patent application or any patent issued thereon.

Respectfully submitted,

Richard W. Scott, Ph.D.

Date: 06/20/2011

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Appendix A

Exhibit 1	Curriculum Vitae for Dr. Richard W. Scott
Exhibit 2	Excerpt from the PolyMedix website, "History," from http//:www.polymedix.com/history.php downloaded 6/9/2011
Exhibit 3	PolyMedix Press Release dated November 16, 2010
Exhibit 4	PolyMedix Press Release dated November 3, 2010
Exhibit 5	PolyMedix Press Release dated September 30, 2010
Exhibit 6	PolyMedix Press Release dated July 27, 2009
Exhibit 7	PolyMedix Press Release dated July 23, 2009
Exhibit 8	PolyMedix Press Release dated June 2, 2009
Exhibit 9	Langreth, R., "Antibiotic Artisan," *Forbes*, 187:42-44 (February 14, 2011)
Exhibit 10	Tew, G.N., *et al.*, *PNAS* 99:5110-5114 (2002)
Exhibit 11	U.S. Patent No. 7,173,102 B2
Exhibit 12	PolyMedix Press Release dated November 23, 2010
Exhibit 13	Curriculum Vitae for Dr. William F. DeGrado
Exhibit 14	Curriculum Vitae for Dr. Michael L. Klein
Exhibit 15	Curriculum Vitae for Gregory Tew

Exhibit 1

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Richard W. Scott	Vice President, Research
eRA COMMONS USER NAME RSCOTT	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(If applicable)*	YEAR(s)	FIELD OF STUDY
Muhlenberg College, Allentown, PA	B. S. (honors)	1971-1975	Biology
University of Pennsylvania, Philadelphia, PA	Ph. D.	1975-1979	Microbiology

A. PERSONAL STATEMENT

As Vice president of Research at PolyMedix, Inc. I have led research teams responsible for the identification and selection of two lead compounds that have successfully completed human Phase 1 clinical studies and are now in Phase 2 trials. Both leads have emerged from discovery programs at PolyMedix that are based on the design of small non-peptidic mimics of protein structure and function. The goal of our synthetic approach is to capture the structural and biological properties of the target proteins on a small, fully synthetic framework amenable to medicinal chemistry. These foldamer mimetics have several advantages over peptides because of their small size, which increases stability and enhances tissue distribution, and ability to fine-tune their physical properties for optimization of potency and safety. The two clinical stage programs are developing foldamer mimetics of 1) anti-thrombin as heparin antagonists and 2) the host defense proteins as anti-microbial agents. In the anti-heparin program, research is directed toward expanding the use of the mimetic antagonists to other heparins and heparin-like drugs, including the low molecular weight heparins and the pentasaccharide, fondaparinux. In the anti-microbial program, research is focused on developing mimetics for other indications, including biofilm-associated infections, surgical site infections and infections caused by multi-drug resistant Gram-negative organisms, biowarfare pathogens, and food-borne pathogens. In addition, the anti-microbial compounds appear to have anti-inflammatory properties. We are beginning to explore indications where a combination of these two properties may be desired, such as oral mucositis.

B. APPOINTMENTS:

1980 - 84: Postdoctoral Trainee and Fellow with Dr. Shirley M. Tilghman, Fox Chase Cancer Center, Philadelphia, PA
1985- 90: Principal Investigator, Central Research and Development, E. I. DuPont deNemours
1/ 1991- 6/91:Senior Scientist, Biochemistry, Cephalon, Inc
1991- 95: Director, Molecular Biology, Cephalon, inc
1995- 98: Senior Director, Molecular Biology, Cephalon, Inc
1998 - 2000: Vice President, Neurobiology, Cephalon, inc
2000- 01: Cephalon Fellow, Cephalon, Inc
11/01 to 11/02: Director, Center for Technology Transfer, University of Pennsylvania
12/02 to present: Vice President, Research, PolyMedix, Inc.

C. HONORS/AWARDS:

1975 - 1977: Microbiology Training Grant Predoctoral Fellowship
1977 - 1979: Analysis of Development Predoctoral Training Grant
1980 - 1981: National Research Service Award Postdoctoral Training Grant
1981 - 1984: National Research Service Award Postdoctoral Fellowship

D. Selected Peer-Reviewed Publications (40 of 58).

Ingram, R.S., R.W. Scott & S.M. Tilghman. 1981. Alpha-fetoprotein and albumin genes are in tandem in the mouse genome. Proc. Natl. Acad. Sci. USA 78: 4694-4698.

Eiferman, F.A., P.R. Young, R.W. Scott & S.M. Tilghman. 1981. Intragenic amplifications and divergence in the mouse a-fetoprotein gene. Nature (London) 294: 713-718.

Scott, R.W. and S. M. Tilghman. 1983. Transient expression of a mouse alpha-fetoprotein minigene: deletion analyses of promoter function. Mol Cell. Biol. 3: 1295-1309.

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Tilghman, S.M., R. W. Scott, T. F. Vogt, R. Krumlauf, R. W. Hamer, and R. Brinster. 1985. Tissue-specific expression of cloned alpha-fetoprotein genes in teratocarcinoma cells and mice. Genetic Manipulation of the Mammalian Ovum and Early Embryos. Cold Spring Harbor Laboratory Press. pg. 21.

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Meyer, S. L., D. M. Lang, M. E. Forbes, E. Knight, Jr., J. D. Hirsch, S. P. Trusko, and R. W. Scott. 1994. High-level production and characterization of recombinant mouse brain-derived neurotrophic factor and rat neurotrophin-3 expressed in insect cells. J. Neurochem. 62: 825-833.

Howland, D. S., M. J. Savage, F. A. Huntress, R. E. Wallace, D. A. Schwartz, T. Loh, R. H. Melloni Jr., L. J. Degennaro, B. D. Greenberg, R. Siman, M. E. Swanson, and R. W. Scott. 1995. Mutant and native human ß-amyloid precursor proteins in transgenic mouse brain [open peer commentary]. Neurobiol. Aging 16: 685-699.

Meyer, S. L., D. Bozyczko-Coyne, S. K. Mallya, C. M. Spais, R. Bihovsky, J. K. Kawooya, D. M. Lang, R. W. Scott, and R. Siman. 1996. Biologically-active monomeric and heterodimeric recombinant human calpain I produced using the baculovirus expression system. Biochem. J. 314: 511-519.

Greenberg, B. D., M. J. Savage, D. S. Howland, S. A. Ali, S. L. Seidlak, G. Perry, R. Siman, and R. W. Scott. 1996. APP transgenesis: approaches toward the development of animal models for Alzheimer disease neuropathology. Neurobiol. Aging 17: 153-171.

Reaume, A. G., J. L. Elliott, E. K. Hoffman, N. W. Kowall, R. J. Ferrante, D. F. Siwek, H. M. Wilcox, D. G. Flood, M. F. Beal, R. H. Brown, Jr., R. W. Scott, and W. D. Snider. 1996. Motor neurons in Cu/Zn superoxide dismutase-deficient mice develop normally but exhibit enhanced cell death after axonal injury. Nature Genetics 13: 43-47.

Hoffman E. K., H. Wilcox, R. Scott, and R. Siman. 1996. Proteosome inhibition enhances the stability of Cu/Zn superoxide dismutase with mutations linked to familial amytrophic lateral sclerosis. J. Neurol. Sci. 139: 15-20.

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SBIR Phase 2: 2 R44 AI058407-02-04 NIAID; Therapeutic Development of Antimicrobial Biomimetics
- PI: Richard W. Scott
- Period: 03/01/06 to 02/28/09
- Goal: Identify and develop IV clinical lead to treat Staphylococcal infections

SBIR Phase 1: R43HL090113-01 NHLBI; Development of Biomimetic Oligomers as Anti-coagulant antagonists
- PI: Richard W. Scott
- Period: 09/21/07 to 09/30/08
- Goal: Identify preclinical development lead as antagonist of unfractionated heparin.

SBIR Phase 1: R43DE018371-01A2 NIAID; A Novel Antimicrobial Peptide Mimetic For Oral Candidiasis
- PI: Richard W.Scott
- Period: 05/12/08 to 04/30/09
- Goal: Identify potent and selective compounds against oral Candida pathogens

SBIR Phase 2: R43HL090113-02 NHLBI; Development of Biomimetic Oligomers as Anti-coagulant antagonists
- PI: Richard W. Scott
- Period: 05/01/09 to 04/30/11
- Goal: Identify development lead compounds as antagonists of low molecular weight heparins.

NIH-Cooperative Research Partnerships for Biodefense and Emerging Infectious Disease; RFA-AI-08-001
- PI: Tew, Gregory; Univ. Of Mass., Amherst, MA
- Period: 04/01/2009 – 03/31/2014
- Role: Manage in vitro and in vivo antimicrobial assays and drug development studies
- Goal: Identify and develop clinical lead to treat illnesses caused by food-borne pathogens

HDTRA1-09-C-0005: DTRA Office of Research and Innovation; Novel Therapeutics to Combat Biowarfare Pathogens
- PI: Scott, Richard W., PolyMedix, Inc.
- Period: 06/01/2009 – 05/31/2010
- Goal: Devise more effective rapid-response countermeasures to biowarfare bacterial pathogens and other public health threats. Generate preclinical efficacy data in rodent models of biopathogen infection.

STTR N09-T033; The United States Office of Naval Research (ONR); Novel Antibacterial Agents
- PI: Scott, Richard W., PolyMedix, Inc.
- Period: 07/01/2009 – 12/31/2009
- Goal: Identify potently active and selective compounds against panels of bacterial pathogens.

STTR A09A-T004-0108 US Army Research Office; Biomimetics for Treating Biofilm-Embedded Infections.
- PI: Scott, Richard W., PolyMedix, Inc.
- Period: 09/01/2009 – 02/28/2010
- Goal: Identify potently active and selective compounds against panels of bacterial pathogens common in biofilm infections.

SBIR Phase 1: National Science Foundation; Development of Antimicrobial Sutures.
- PI: Scott, Richard W., PolyMedix, Inc.
- Period: 07/01/2010 – 12/31/2010
- Goal: Production of efficacious and safe prototype antimicrobial sutures.

SBIR Phase 1 (Fast-track): 1R44AI090762-01 NIAID; Development of Small Antimicrobial Peptide Mimetics as Drug-Resistant and Susceptible Antimalarial Therapeutics
- PI: Scott, Richard W., PolyMedix, Inc. (co-PI).
- Period: 07/15/2010 – 06/30/2012
- Goal: Identification of lead compounds efficacious against *P. falciparum* in malaria animal models.

STTR Phase 2 W911NF-10-C-0111 US Army Research Office; Biomimetics for Treating Biofilm-Embedded Infections.
- PI: Scott, Richard W., PolyMedix, Inc.
- Period: 09/01/2010 – 08/31/2012
- Goal: Identify potently active and selective compounds against panels of bacterial pathogens common in biofilm infections.

Exhibit 2

PolyMedix®
Revolutionizing the Treatment of Serious Infectious Diseases & Cardiovascular Disorders with Biomimetics

PolyMedix develops biomimetics - novel small molecule drugs which mimic the activity of proteins. These are designed with a proprietary computational technology platform.

History

PolyMedix was founded in 2002, based on proprietary computational drug design technology which we have exclusively licensed from the University of Pennsylvania. This technology is based on the work of Drs. William DeGrado and Michael Klein, who are members of the National Academy of Sciences, the American Academy of Arts and Sciences, and the Royal Society. Our proprietary de novo drug design approach involves using protein targets with well-understood physical structures and biological activity, and designing small molecule compounds that mimic or regulate the activity of these targets. We believe our structure-based approach allows us to rationally design novel product candidates and greatly improve the efficiency of new drug discovery.

Scientific Founders and Advisors

Dr. William DeGrado is Raizus Professor of Biochemistry and Biophysics at the Medical School of the University of Pennsylvania, has over 250 publications and a multitude of patents. He is a member of the National Academy of Sciences and the American Academy of Arts and Sciences, and has earned the prestigious Merryfield and Hirschman Chemistry Awards.

Dr. Michael Klein is Director of the prestigious Laboratory for Research on the Structure of Matter at the University of Pennsylvania, and has over 500 publications over the past 40 years. He is a member of the Royal Society and the American Academy of Arts and Sciences.

Dr. Gregory Tew is Associate Professor at the School of Polymer Sciences and Engineering at the University of Massachusetts. He is an expert in polymeric materials science, and recipient of numerous awards including the PECASE.

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Exhibit 3

PolyMedix®
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Press Releases

PolyMedix and University of Massachusetts Receive $750,000 Contract from U.S. Army Research Office

Supports Continued Development of Novel Antibacterial Compounds Against Drug Resistant Bacterial Biofilms

Radnor, PA (November 16, 2010) - PolyMedix, Inc. (OTC BB: PYMX), an emerging biotechnology company focused on developing new therapeutic drugs to treat infectious diseases and acute cardiovascular disorders, and the University of Massachusetts, Amherst (UMass), have received a Phase 2 Small Business Technology Transfer (STTR) contract in the amount of $750,000. This contract will allow PolyMedix to conduct further testing on antimicrobial compounds which PolyMedix identified under the initial Phase 1 contract. These compounds are being developed to specifically treat multi-drug resistant biofilm-embedded bacteria. This award represents the 15th grant or research contract received to date by PolyMedix.

This two-year contract is sponsored by the U.S. Army Research Office. Under this Phase 2 STTR contract, PolyMedix and UMass will conduct further research and analysis, including in vitro and proof of concept in vivo studies, to identify lead small molecule defensin-mimetic antimicrobial compounds active against bacterial pathogens associated with biofilm infections. PolyMedix expects to receive $524,000 under this contract.

"We appreciate the continued interest of the U.S. Army Research Office, and granting us this contract which allows us to expand upon our research conducted under the Phase 1 portion that we received in August 2009," commented Dr. Richard Scott, Vice President of Research at PolyMedix. "Biofilm infections can be serious and life-threatening. We believe that our small molecule defensin-mimetics, with their completely different mechanism of action that is intended to make bacterial resistance unlikely to develop, could be an important advance in addressing biofilm infections. We look forward to continuing to work with the U.S. Army to develop our compounds for military applications and to safeguard our all-important armed services."

There is a growing need to develop new drugs and therapies to combat biofilm infections. Biofilms form when certain microorganisms, such as bacteria, adhere to living or non-living surfaces and begin to reproduce. Biofilms can form on just about any material or surface including metals, plastics, prosthesis, medical implants such as knee and hip replacements, and human tissue. When a biofilm forms on an infection, treatment becomes very complicated as biofilms enable bacteria to survive making them more resistant to antibiotics.

PolyMedix's small molecule defensin-mimetic antimicrobial compounds are designed to mimic human host defense proteins, the body's natural defense against bacterial infections. Host defense proteins use a simple, but effective method for killing bacteria and other microbes by targeting the microbial membranes and disrupting them. This mechanism of action is intended to make it difficult for resistance to develop.

PolyMedix's lead small molecule defensin-mimetic antibiotic compound is PMX-30063. PolyMedix has recently initiated a Phase 2 clinical trial in Canada to evaluate the safety and efficacy of PMX-30063 in patients as a treatment for Acute Bacterial Skin and Skin Structure Infections (ABSSSI) caused by *Staph* bacteria. Results from two Phase 1 studies demonstrated that PMX-30063 could be safely administered in single or divided intravenous doses, at levels that exceeded theoretical efficacious levels predicted by animal models. In addition, PMX-30063 killed *Staph* bacteria, including MRSA, in human serum in blood samples drawn from subjects in the study.

This project is supported in part by the U.S. Army Research Office. The content of this press release does not necessarily reflect the position or the policy of the Government, and no official endorsement should be inferred.

About PolyMedix, Inc.
PolyMedix is a publicly traded biotechnology company focused on the development of novel drugs for the treatment of serious infectious diseases and acute cardiovascular disorders. PolyMedix uses a rational drug design approach to create non-peptide small molecule drug candidates. PMX-30063, PolyMedix's lead antibiotic compound that is currently in Phase 2 clinical trials, is a small molecule that mimics human host-defense proteins and has a mechanism of action distinct from those of current antibiotic drugs, a mechanism which is intended to make bacterial resistance unlikely to develop. PolyMedix plans to develop this

compound for serious systemic Staphylococcal infections, including methicillin resistant Staphylococcus aureus (MRSA). PMX-60056, PolyMedix's lead heptagonist compound, has completed four clinical trials and is being further developed to reverse the anticoagulant activity of both heparin and low molecular weight heparins. PolyMedix believes that PMX-60056 could potentially be a safer and easier to use anticoagulant reversing agent, with broader activity, than the currently approved therapy for reversing heparin. PolyMedix also plans to continue the development of its PolyCides®, polymeric formulations as antimicrobial biomaterials, which can be used as additives to paints, plastics, and textiles to create self-sterilizing products and surfaces. For more information, please visit our website at www.polymedix.com.

This press release contains forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 that involve risks, uncertainties and assumptions that could cause PolyMedix's actual results and experience to differ materially from anticipated results and expectations expressed in those forward looking statements. PolyMedix has in some cases identified forward-looking statements by using words such as "anticipates," "believes," "hopes," "estimates," "looks," "expects," "plans," "intends," "goal," "potential," "may," "suggest," and similar expressions. Among other factors that could cause actual results to differ materially from those expressed in forward-looking statements, PolyMedix's compounds may not successfully complete clinical testing, or be granted regulatory approval to be sold and marketed in the United States or elsewhere. A more complete description of these risk factors is included in PolyMedix's filings with the Securities and Exchange Commission. You should not place undue reliance on any forward-looking statements. PolyMedix undertakes no obligation to release publicly the results of any revisions to any such forward-looking statements that may be made to reflect events or circumstances after the date of this press release

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Exhibit 4

PolyMedix®
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Print Window

Press Releases

PolyMedix Awarded Therapeutic Discovery Credits for Two Lead Programs
Receives Approximately $500,000

Radnor, PA (November 03, 2010) - PolyMedix, Inc. (OTC BB: PYMX), a biotechnology company focused on developing new therapeutic drugs to treat infectious diseases and acute cardiovascular disorders, announced today that it has been awarded two cash grants totaling $488,958 under the U.S. Government's Qualifying Therapeutic Discovery Project (QTDP) program. Eligibility for the grant requires that a project: have the potential to develop new treatments that address "unmet medical needs" or chronic and acute diseases; reduce long-term health care costs; or represent a significant advance in finding a cure for cancer.

PolyMedix applied for two projects, both of which qualified and received the maximum grant amounts, including:

- PMX-30063, novel defensin-mimetic antibiotic compound. PolyMedix has recently initiated a Phase 2 clinical trial in Canada to evaluate the safety and efficacy of PMX-30063 in patients as an initial treatment for Acute Bacterial Skin and Skin Structure Infections (ABSSSI) caused by *Staph*.
- PMX-60056, synthetic small-molecule anticoagulant reversing agent. PolyMedix has completed four Phase 1 clinical trials evaluating the safety and efficacy of PMX-60056 in reversing heparin and low molecular weight heparins. PolyMedix is preparing to initiate a Phase 2 clinical trial in Percutaneous Coronary Intervention (PCI) patients later this year or early next year.

The QTDP program was created by Congress as part of the Patient Protection and Affordable Care Act of 2010. Allocation of the credit also takes into consideration which projects show the greatest potential to create and sustain high-quality, high-paying U.S. jobs and to advance U.S. competitiveness in life, biological and medical sciences. The credit is only available to companies with no more than 250 employees.

About PolyMedix, Inc.
PolyMedix is a publicly traded biotechnology company focused on the development of novel drugs for the treatment of serious infectious diseases and acute cardiovascular disorders. PolyMedix uses a rational drug design approach to create non-peptide small molecule drug candidates. PMX-30063, PolyMedix's lead antibiotic compound that is currently in Phase 2 clinical trials, is a small molecule that mimics human host-defense proteins and has a mechanism of action distinct from those of current antibiotic drugs, a mechanism which is intended to make bacterial resistance unlikely to develop. PolyMedix plans to develop this compound for serious systemic Staphylococcal infections, including methicillin resistant Staphylococcus aureus (MRSA). PMX-60056, PolyMedix's lead heptagonist compound, has completed four clinical trials and is being further developed to reverse the anticoagulant activity of both heparin and low molecular weight heparins. PolyMedix believes that PMX-60056 could potentially be a safer and easier to use anticoagulant reversing agent, with broader activity, than the currently approved therapy for reversing heparin. PolyMedix also plans to continue the development of its PolyCides®, polymeric formulations as antimicrobial biomaterials, which can be used as additives to paints, plastics, and textiles to create self-sterilizing products and surfaces. For more information, please visit our website at www.polymedix.com.

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Exhibit 5

PolyMedix®

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Press Releases

PolyMedix Receives Phase 2 NIH Grant to Develop a Novel Antimicrobial Defensin Mimetic for Oral Candidiasis

$1 Million in Research Funding Over Two Years

Radnor, PA (September 30, 2010) - PolyMedix, Inc. (OTC BB: PYMX), an emerging biotechnology company focused on developing new therapeutic drugs to treat acute cardiovascular disorders and infectious diseases, has received a Phase 2 grant in the amount of $986,000 from the National Institute of Health (NIH) to support the development of defensin mimetic antimicrobial compounds for the treatment of oral candidiasis. This grant will fund this research project through August 31, 2012. This award represents the 14th grant or research contract received to date by PolyMedix.

This is the second grant received from the NIH for the treatment of oral candidiasis. Under the first portion of this grant, which was awarded in 2008, PolyMedix identified several small molecule defensin mimetic compounds with activity against Candida. The primary goal of this grant is to determine the optimal compounds and conditions under which PolyMedix's defensin mimetic antimicrobials can be applied to oral mucosa in order to efficiently clear an oral Candida infection. The goal of this phase is to provide a development lead candidate for further development as a topical treatment for oral candidiasis. Working with PolyMedix on this grant is Gill Diamond, Ph.D., Associate Professor, Department of Oral Biology at University of Medicine and Dentistry of New Jersey.

"Oral Candidiasis is a common infection of the oral cavity caused by an overgrowth of the yeast fungus, Candida," commented Richard Scott, Ph.D., Vice President for Research at PolyMedix. "We believe our small molecule defensin mimetic compounds represent a novel approach to developing new agents to treat these painful and sometimes life-threatening infections, with the important advantage of limited opportunity for the development of resistance. Several of our defensin-mimetic antimicrobial compounds have demonstrated promising activity against fungal strains that often cause human infectious diseases and are resistant to existing anti-fungal agents. With this funding from the NIH we are able to continue our research in developing a compound to potentially address this major medical need."

PolyMedix's small molecule defensin-mimetic antimicrobial compounds are designed to mimic human host defense proteins, the body's natural defense against bacterial infections. Host defense proteins use a simple, but effective method for killing bacteria and other microbes by targeting the microbial membranes and disrupting them. This mechanism of action makes it difficult for resistance to develop.

PolyMedix's lead small molecule defensin-mimetic antibiotic compound is PMX-30063. PolyMedix has recently initiated a Phase 2 clinical trial in Canada to evaluate the safety and efficacy of PMX-30063 in patients as an initial treatment for Acute Bacterial Skin and Skin Structure Infections (ABSSSI) caused by *Staph*. Results from two Phase 1 studies demonstrated that PMX-30063 could be safely administered in single or divided IV doses, at levels that exceeded theoretical efficacious levels predicted by animal models. In addition, PMX-30063 killed *Staph* bacteria, including MRSA, in human serum in blood samples drawn from subjects in the study.

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Exhibit 6

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Print Window

Press Releases

POLYMEDIX AND UNIVERSITY OF MASSACHUSETTS AMHERST RECEIVE UP TO $6.6 MILLION NIH GRANT TO DEVELOP NEW ANTIBIOTICS

Project to develop new defensin-mimetic antimicrobial compounds for biodefense and emerging food-borne infectious diseases
PolyMedix to receive up to $3.5 million in funding over 5 years

Radnor, PA (July 27, 2009) - PolyMedix, Inc. (OTC BB: PYMX), an emerging biotechnology company developing acute care products for infectious diseases and acute cardiovascular disorders, and the University of Massachusetts at Amherst, Department of Polymer Sciences and Engineering, announced today that they have received a NIH grant to support the development of antimicrobial defensin-mimetic compounds for biodefense and emerging food-borne infectious diseases.

The sponsoring agency for the grant is Cooperative Research Partnerships for Biodefense and Emerging Infectious Disease of the National Institutes of Health. The grant provides PolyMedix and the University of Massachusetts $977,658 for one year, of which PolyMedix expects to receive $265,539. The grant recommends funding for an additional four years, subject to availability of funds and satisfactory performance, which brings the potential value of the grant up to an aggregate of $6.6 million over the five year period. The amount of support expected to be received by PolyMedix is up to $3.5 million over the five year period, and is planned to support three scientific staff. The primary goal of the grant is to characterize PolyMedix's antimicrobial defensin mimetic compounds and develop a clinical lead candidate for treating food-borne illnesses with an emphasis on Gram-negative bacteria. The principal investigator at the University of Massachusetts for the grant is Dr. Gregory Tew, Professor at the Department of Polymer Sciences and Engineering, and a scientific founder of PolyMedix.

"This grant will allow us to expand the chemical landscape of antimicrobial peptide mimics with a focus on important food-borne illnesses caused by Gram-negative pathogens. It also represents an outstanding relationship between the University of Massachusetts and PolyMedix", said Dr. Gregory Tew of the University of Massachusetts.

"We greatly appreciate the continued support of NIH and their recognition of the significance of our novel antibiotic compounds and drug discovery technology," said Nicholas Landekic, President and C.E.O of PolyMedix. "This award could enable the development of the next generations of novel antibiotics for drug resistant bacteria and emerging infections. This grant represents the tenth outside funding received by PolyMedix and supports work that we would otherwise not be in a position to pursue at this time. We are proud to receive this important grant and to continue our work with the University of Massachusetts and Dr. Gregory Tew".

PolyMedix's lead defensin-mimetic antibiotic compound is PMX-30063, currently in Phase I clinical development. On December 10, 2008 PolyMedix announced the results of the first Phase I human clinical study with PMX-30063. The results of that study suggest that it should be possible to achieve clinically therapeutic levels with daily doses of PMX-30063 which are lower than those associated with any adverse effects seen in the single dose study. On June 5, 2009 PolyMedix announced that it had initiated dosing in a second clinical study with PMX-30063. This Phase IB clinical study will assess the safety of PMX-30063 given repeatedly over a period of several days. The initial indication planned for PMX-30063 is as a treatment for pan-Staphylococcal infections, including MRSA (methicillin-resistant *Staphylococcus aureus*).

About PolyMedix, Inc.
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biomaterials, which can be used as additives to paints, plastics, and textiles to create self-sterilizing products and surfaces. For more information, please visit our website at www.polymedix.com.

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Exhibit 7

PolyMedix®

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Press Releases

POLYMEDIX AND UNIVERSITY OF MASSACHUSETTS RECEIVE UP TO $100,000 CONTRACT TO DEVELOP NOVEL ANTIBACTERIAL COMPOUNDS AGAINST PATHOGENS OF MILITARY INTEREST

Contract Supported by the Office of Naval Research

Radnor, PA (July 23, 2009) - PolyMedix, Inc. (OTC BB: PYMX), an emerging biotechnology company developing acute care products for infectious diseases and acute cardiovascular disorders, and the University of Massachusetts, have received a Phase I Small Business Technology Transfer (STTR) contract in the amount of up to $99,838, to support research to identify lead antimicrobial compounds against bacterial pathogens most relevant to the military, with a particular focus on *Acinetobacter*.

The sponsoring agency for this contract is the Office of Naval Research (ONR). The primary goal of the work funded by this Phase I STTR contract will be to discover lead antimicrobial compound(s) based on PolyMedix's novel small molecule defensin-mimetics for activity against bacterial pathogens most relevant to the military, with a particular focus on *Acinetobacter*. *Acinetobacter* is a Gram-negative bacteria which can cause pneumonia, and is highly refractory to currently available antibiotic drugs. PolyMedix will receive $69,890 in the first phase of the contract, to be disbursed over six months, with an optional extension which may provide an additional $29,948 of funding for continued work which would be done together with Dr. Gregory Tew of the University of Massachusetts Amherst.

This contract represents the ninth outside supported funding, in the form of a grant or research contract, and the third related to biodefense, received by PolyMedix. On June 2, 2009 PolyMedix announced that it had received a $1.6 million contract from the Defense Threat Reduction Agency (DTRA) to develop new antibiotic compounds based on its proprietary defensinmimetics to combat biowarfare pathogens. In September 2004 PolyMedix received a Phase I SBIR grant from the National Institutes of Health (NIH) in the amount of $167,000 to study its novel defensin-mimetic antibiotic compounds against anthrax and other biowarfare pathogens. The results of that work suggest that certain of PolyMedix's antimicrobial compounds demonstrated antimicrobial activity in test-tube experiments against the infectious agents, which cause anthrax, plague, tularemia, and listeriosis.

PolyMedix's lead defensin-mimetic antibiotic compound is PMX-30063, currently in Phase I clinical development. On December 10, 2008, PolyMedix announced the results of the first Phase I human clinical study with PMX-30063. The results of that study suggest that it should be possible to achieve clinically therapeutic levels with daily doses of PMX-30063 which are lower than those associated with any adverse effects seen in the single dose study. On June 5, 2009, PolyMedix announced that it had initiated dosing in a second Phase I clinical study with PMX-30063. This Phase IB clinical study will assess the safety of PMX-30063 given repeatedly over a period of several days. The initial indication planned for PMX-30063 is as a treatment for pan-Staphylococcal infections, including MRSA (methicillin-resistant *Staphylococcus aureus*).

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Exhibit 8

PolyMedix®
Revolutionizing the Treatment of Serious Infectious Diseases & Cardiovascular Disorders with Biomimetics

Print Version

Press Releases

POLYMEDIX RECEIVES $1.6 MILLION CONTRACT FROM THE DEFENSE THREAT REDUCTION AGENCY (DTRA) TO DEVELOP ANTIBIOTIC COMPOUNDS TO COMBAT BIOWARFARE PATHOGENS

Goal To Devise More Effective Rapid-Response Countermeasures

Radnor, PA (June 02, 2009) - PolyMedix, Inc. (OTC BB: PYMX, an emerging biotechnology company developing acute care products for infectious diseases and acute cardiovascular disorders, has received a research contract from the Defense Threat Reduction Agency (DTRA) in the amount of $1.6 million to develop new defensin-mimetic antibiotic compounds to combat biowarfare pathogens.

The sponsoring agency for this research contract is the DTRA. The research contract provides $1.6 million of support to PolyMedix over one year. The research contract will support four scientific staff at PolyMedix. The primary goal of the contract is to devise more effective rapidresponse countermeasures against biowarfare bacterial pathogens and other public health threats. The work to be conducted by PolyMedix will include preclinical animal efficacy studies for intravenous defensin-mimetic antibiotic agents against Category A and B biopathogens, including the infectious agents which cause anthrax, plague, and tularemia.

In September 2004 PolyMedix received a Phase I SBIR grant from the National Institutes of Health (NIH) in the amount of $167,000 to study its novel defensin-mimetic antibiotic compounds against anthrax and other biowarfare pathogens. The results of that work suggest that certain of PolyMedix's antimicrobial compounds demonstrated antimicrobial activity in test-tube experiments against the infectious agents, which cause anthrax, plague, tularemia, and listeria.

"This award represents the seventh outside supported funding received by PolyMedix, and the second related to biodefense," said Nicholas Landekic, President and C.E.O. of PolyMedix. "We appreciate the DTRA's interest in our novel antibiotic approach, and look forward to continuing this work and identifying new generations of antimicrobial compounds. Safeguarding public safety against these dangerous infectious threats is a critically important goal."

PolyMedix's lead defensin-mimetic antibiotic compound is PMX-30063, currently in Phase I clinical development. On December 10, 2008, PolyMedix announced the results of the first Phase I human clinical study with PMX-30063. The results of that study suggest that it should be possible to achieve clinically therapeutic levels with daily doses of PMX-30063 which are lower than those associated with any adverse effects seen in the single dose study. On May 15, 2009, PolyMedix announced that it had received regulatory clearance from Health Canada to initiate a second Phase I clinical study with PMX-30063. This Phase IB clinical study will assess the safety of PMX-30063 given repeatedly over a period of several days. The initial indication planned for PMX-30063 is as a treatment for pan-Staphylococcal infections, including MRSA (methicillin-resistant *Staphylococcus aureus*).

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Exhibit 9

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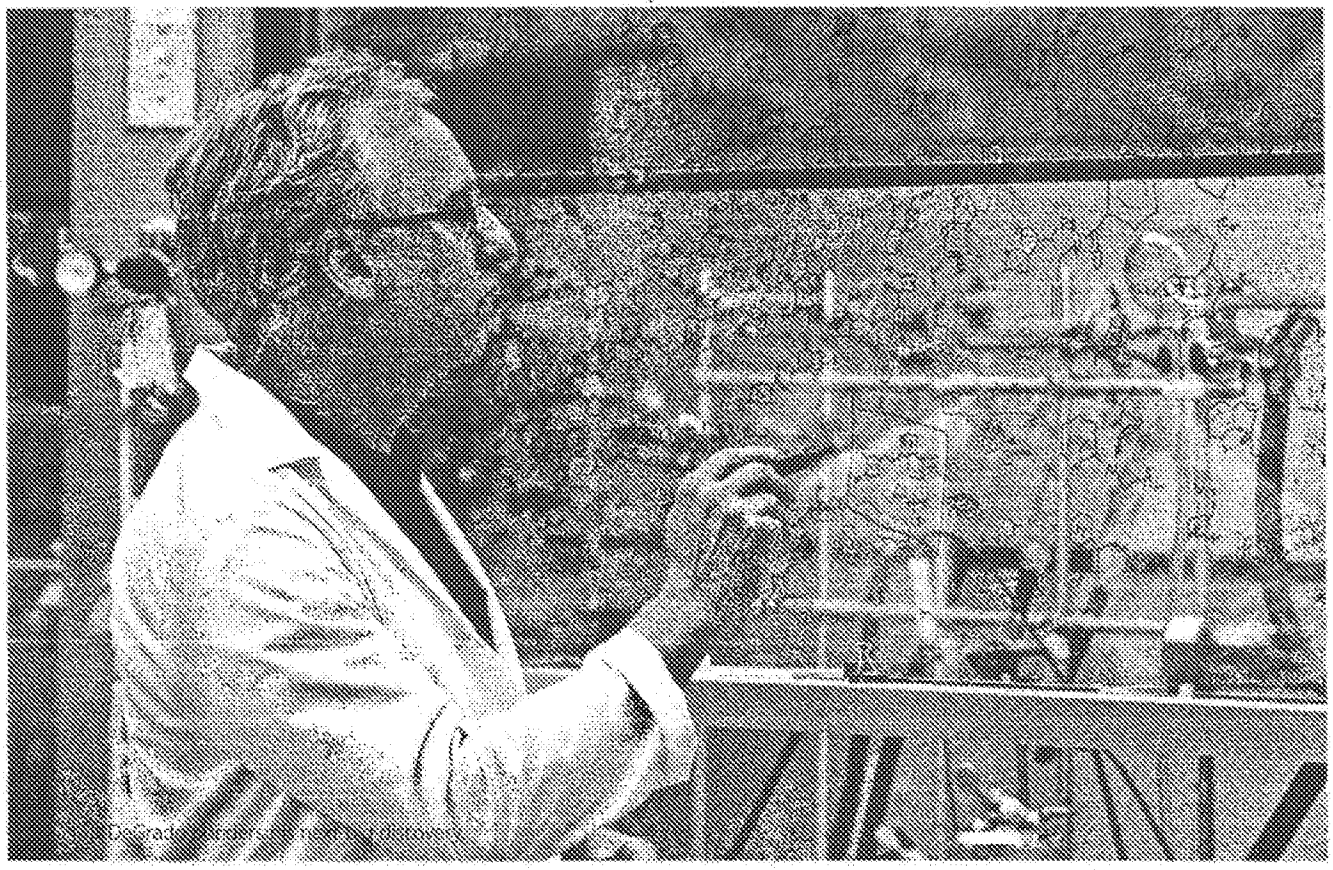

Antibiotic Artisan

Using supercomputer simulations, chemist William DeGrado is crafting potent new drugs that mimic nature's own defenses.

BY ROBERT LANGRETH

The biotech industry creates new drugs by making tweaks to natural proteins. University of Pennsylvania chemist William DeGrado is more of an artist than a tweaker. He has spent much of his career designing new proteins from scratch, a three-dimensional engineering task so complicated that until recently few scientists bothered to try. His goal is to create molecules unknown to nature but adept at serving humans by absorbing environmental toxins, fighting cancer or extending Moore's Law down to the atomic scale.

These applications are years away. But DeGrado's interest in creating artificial molecules that mimic more complex natural ones may have a more immediate payoff: a powerful new generation of antibiotics.

Scientists have known for decades that organisms as diverse as insects, frogs, pigs and humans make natural protein-based antibiotics to ward off microbes. These chemicals are one of

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life's most ancient defenses. They attack microbes in a unique way that makes it hard for resistance to develop.

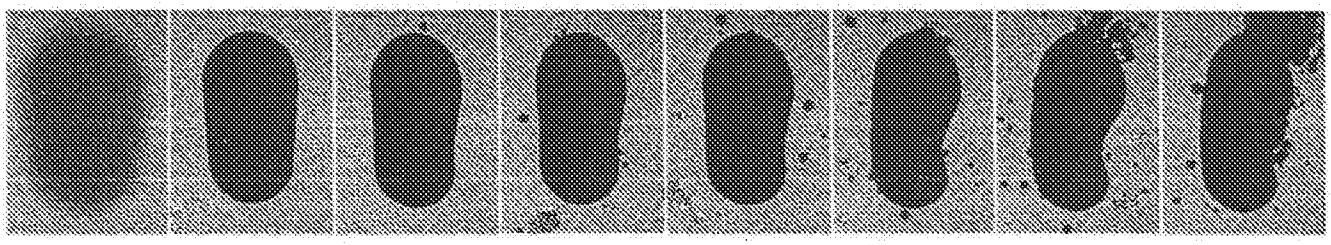
Drugmakers have tried to bottle their power, but the compounds, known as antimicrobial peptides, have proven to be poor drugs. They are difficult to manufacture, unstable in the bloodstream and prone to toxic side effects. A drug based on pig chemicals failed to prevent pneumonia in hospital patients in a 2006 study. Another drug, from the African clawed frog, was rejected in 1999 by the FDA as a treatment for diabetic foot ulcers. Because of the peptides' high cost and unclear safety profile, "Big Pharma has abandoned them," says Georgetown University researcher Michael Zasloff.

DeGrado, with the help of a powerful supercomputer simulation, has created new antibiotics that mimic natural ones but are far simpler to produce and more stable. They capture the essence of animal antibiotics in molecules that are one-quarter the size and can be made with standard chemistry techniques. The supercomputer work "was absolutely critical" in crafting the antibiotic, says DeGrado. "It narrowed the choices tremendously [and converted it] from an intractable problem to a feasible one."

other things, helps it to distinguish bacteria from human membranes, which have a less negative charge. The other side of the antibiotic contains an oily surface that is attracted to the greasy interior portion of the membrane.

Doodling on a scrap of paper with postdoctoral student Gregory Tew (now a professor at the University of Massachusetts), DeGrado came up with a crescent-shaped molecule that was somewhat similar to the polymer Kevlar used in bulletproof vests. He wasn't sure it would work, so he took it across the campus to molecular modeling expert Michael Klein. Klein took one look and was convinced that DeGrado was on to something. "I was so excited that I got [DeGrado] to sign and date the paper and gave it to my secretary" for safekeeping, recalls Klein, now at Temple University.

Klein devised a supercomputer simulation to predict in practically atomic detail what would happen when DeGrado's molecule collided with a bacterium's membrane. Each "frame" of the movie represents a fraction of a nanosecond and involves 1 million calculations. The simulation took nearly three months to perform at the Pittsburgh Supercomputing Center and revealed that DeGrado's instincts were on target. "What we discovered with the simulation is that these things dive into the membrane and swim around underneath," says Klein. "When there is enough of them they make their way to the other side of the membrane and make a pore." The bacterium's contents leak out. Lab experiments confirmed that this is what happens.



After a bacterium is hit by PolyMedix's new antibiotic, its membrane is compromised and the contents leak out. This artist's rendition is based on an electron microscope's image of an E. coli bacterium. This mechanism should be less vulnerable to resistance.

The first antibiotic from this work is now in human trials at the biotech firm PolyMedix, which DeGrado cofounded in 2002. In animal tests PolyMedix's drug PMX-30063 is at least as powerful as the gold standard hospital antibiotic vancomycin at killing key strains. The initial effectiveness trial in staph skin infections could yield results this year.

New antibiotics are badly needed as bacteria become resistant to existing drugs. Because existing antibiotics target specific bacterial molecules, a mutation in the bacterium can render the drugs ineffective. One nasty bug inhabiting American hospitals, methicillin-resistant *Staphylococcus aureus*, is linked to 18,650 deaths each year, a 2007 study concluded. In contrast, the peptide antibiotics are less vulnerable to resistance because they infiltrate and damage the membrane that holds the bacterium together.

In 2000 DeGrado became curious about what was the simplest possible molecule that could mimic this membrane-infiltrating ability. He realized that the key was a two-sided structure. One side is attracted to negatively charged molecules on the surface of bacterial membranes. This, among

DeGrado and Klein published their initial results in 2002 and cofounded PolyMedix the same year. It took six years to design and test a molecule safe and effective enough to go into human trials. No resistance to PolyMedix' drug has emerged in standard lab tests. Klein says the continuous simulations give chemists confidence they are on the right track. "Our role is often psychological. A good scientist has intuition. If we can build a model that reinforces that intuition, they have confidence to extrapolate to the next level."

Wall Street remains skeptical. PolyMedix shares hover around a dollar. A key question is whether the drug will be able to distinguish bacteria from host as it goes about its killing business. PolyMedix Chief Executive Nicholas Landekic is optimistic—there have been no showstopper safety problems so far—but only big human trials can tell for sure.

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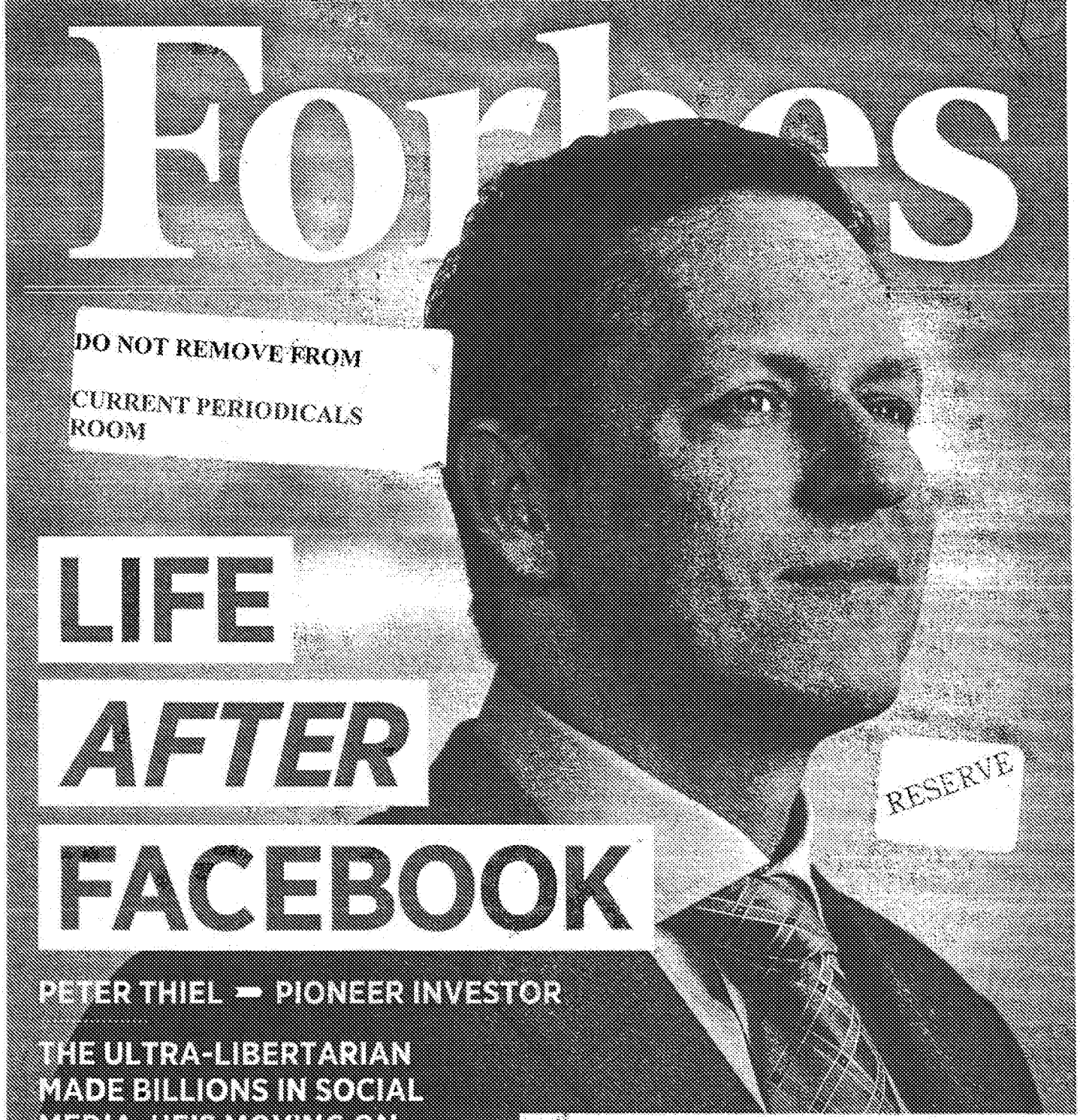

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PETER THIEL — PIONEER INVESTOR

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A BRIEF WORD

Brand Power And Our Path Forward

BY LEWIS D'VORKIN

Over its 93 years as a major force in the media business, FORBES has offered business news consumers authoritative journalism with a clear and strong voice. We are unabashed champions of free enterprise.

The worlds we write about move faster than ever, producing stress and disruption. That includes our very own news industry. The advertising world is changing. New technologies pop up every day. Younger audiences consume news differently. The journalist's role is up for grabs now that anyone can publish anytime.

With change comes opportunity. FORBES understands that. Ten years ago we dove headfirst into the Web while most of Big Media watched and waited. With the rise of social media, we're moving ahead again:

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- We're opening up our print and digital platforms so the three vital voices of the media business—consumers, experienced content creators and our marketing partners—can forge more rewarding relationships with one another.
- We're creating a new architecture for Forbes.com, including revamped home and channel pages, to put first-class journalism at the center of a social media experience.
- We're enhancing production elements of FORBES magazine to complement our recently redesigned pages.

At FORBES we are proud of our heritage, our values and our standards. Our nearly 100-year-old message remains as strong as ever, perhaps more so in a society that increasingly puts its hopes and dreams in the agile thinking of entrepreneurs. As we innovate, we can build the very best products for our loyal FORBES readers—and new ones, too. As it all unfolds, a venerable media brand will grow that much stronger.

Exhibit 10

De novo design of biomimetic antimicrobial polymers

Gregory N. Tew*†‡, Dahui Liu*‡, Bin Chen§, Robert J. Doerksen§, Justin Kaplan*, Patrick J. Carroll¶, Michael L. Klein§, and William F. DeGrado*¶

*Department of Biochemistry and Biophysics, University of Pennsylvania School of Medicine, Philadelphia, PA 19104-6059, and §Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104-6323

Contributed by William F. DeGrado, January 28, 2002

The design of polymers and oligomers that mimic the complex structures and remarkable biological properties of proteins is an important endeavor with both fundamental and practical implications. Recently, a number of nonnatural peptides with designed sequences have been elaborated to provide biologically active structures; in particular, facially amphiphilic peptides built from β-amino acids have been shown to mimic both the structures as well as the biological function of natural antimicrobial peptides such as magainins and cecropins. However, these natural peptides as well as their β-peptide analogues are expensive to prepare and difficult to produce on a large scale, limiting their potential use to certain pharmaceutical applications. We therefore have designed a series of facially amphiphilic arylamide polymers that capture the physical and biological properties of this class of antimicrobial peptides, but are easy to prepare from inexpensive monomers. The design process was aided by molecular calculations with density functional theory-computed torsional potentials. This new class of amphiphilic polymers may be applied in situations where inexpensive antimicrobial agents are required.

A large group of defense peptides, such as the magainins, are produced in eukaryotic systems and provide a first line of defense against bacterial infections (1–4). These peptides adopt facially amphiphilic conformations, in which positively charged and hydrophobic groups segregate onto opposite faces of a helix, sheet, or tertiary structure (Fig. 1) (5, 6). This structural feature is believed to be responsible for their ability to kill cells by disrupting phospholipid membranes.

The activity of this class of peptides depends on its overall physicochemical properties rather than the precise details of its structures (6). Thus, it has been possible to design β-peptides (7–9) and self-assembling cyclic peptides (10) that mimic the biological and physical properties of antimicrobial peptides. An important consideration in the design of antimicrobial β-peptides was to match the hydrophobic period of the sequence with that of the secondary structure adopted by the peptide. For example, C^3-substituted β-peptides adopt a "14-helix" with an approximate 3-residue repeat (11, 12). Thus, oligomers based on a repeating tripeptide sequence, Hb-Hb-Hp (Hb = hydrophobic, Hp = hydrophilic), adopt facially amphiphilic conformations in which apolar and polar side chains segregate onto opposite faces of the helix (7–9, 13). An important extension of this work would be to design inexpensive polymers and oligomers that adopt amphiphilic secondary structures. Such surface-active polymers could be used for a variety of purposes, such as antimicrobial materials and surfaces (14). The fundamental knowledge obtained in these studies would also have important implications for the design of sequence-specific oligomers with well defined three-dimensional structures and biological properties.

Materials and Methods

2,6-Dinitro-4-*t*-butyl-phenyl (4-methyl)-benzenesulfonate (8). 2,6-Dinitro-4-*t*-butyl-phenol (80 mmol) and tosyl chloride (80 mmol) were dissolved in 300 ml of CH_2Cl_2. Diisopropylethylamine (DIEA; 80 mmol) was added to the solution. The mixture was stirred at room temperature for 2 h. The solution was washed with 10% citric acid, saturated aqueous NaCl (sat. NaCl), and dried with $MgSO_4$. The solvent was removed under reduced pressure, and the product was obtained as a bright yellow solid in quantitative yield. MP 145–146°C ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.12 (s, 2H), 7.80 (d, 2H), 7.40 (d, 2H), 2,51(s, 3H), 1.41 (s, 9H). Electrospray ionization-MS: *m/z*: 417.07 (calcd); 417.2 ($M + Na^+$).

2,6-Dinitro-4-*t*-butyl-1-(2-*t*-butoxycarbonylaminoethyl)-sulfanylbenzene (9). Compound **8** (13 mmol), 2-boc-aminoethanethiol (16 mmol), and DIEA (13 mmol) were dissolved in 50 ml of chloroform. The solution was stirred under nitrogen for 12 h. The solution was washed with 0.5 M NaOH, 10% citric acid, saturated (sat.) Na_2CO_3 and sat. NaCl, and dried with $MgSO_4$. The solution volume was reduced to 15 ml by rotary evaporation. The product crystallized as a bright yellow solid after addition of 80 ml of hexane. Yield: 94%. MP 127–129°C ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.81 (s, 2H), 4.87 (s, 1H), 3.31 (t, 2H), 3.10 (t, 2H), 1.44 (s, 9H), 1.39 (s, 9H). Electrospray ionization-MS: *m/z*: 422.45 (calcd); 422.4 ($M + Na^+$).

2,6-Diamino-4-*t*-butyl-1-(2-*t*-butoxycarbonylaminoethyl)sulfanylbenzene (10). Dinitro compound **9** (20 mmol) and sodium acetate (200 mmol) were added to 50 ml of EtOH. The mixture was heated to 78°C, and the solid dissolved completely. $SnCl_2{\cdot}2H_2O$ (200 mmol) was added to the solution, and the reaction mixture was stirred at 78°C for 35 min. After removal of solvent under reduced pressure, the residue was dissolved in 800 ml of EtOAc and washed with 40% K_2CO_3. The solvent was reduced by rotary evaporation, and the product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH 100:1 to 95:5). Yield: 93%. MP 111–113°C ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.21 (s, 2H), 5.41 (s, 1H), 4.35 (br, 4H), 3.21 (t, 2H), 2.75 (t, 2H), 1.35 (s, 9H), 1.24 (s, 9H). Electrospray ionization-MS: *m/z*: 340.51 (calcd); 340.5 (MH^+).

General Method of Polymerization. Diamine **10** (0.1 mmol) was dissolved in 3 ml of dimethylformamide (DMF). Isophthaloyl dichloride (0.1 mmol), triethylamine (0.2 mmol) and *N,N*-dimethylethylenediamine (0.02 mmol for **4** and 0 mmol for **5**) were added while stirring. The mixture was stirred under nitrogen for 18 h. After the volume of solvent was reduced to 1 ml, water was added to precipitate the polymer. The polymer was collected and dried under vacuum. The Boc group was removed by treatment with trifluoroacetic acid (TFA; 3 ml) for 1 h. The deprotected polymer was dried under vacuum overnight.

Solid-Phase Synthesis of Oligomers 2 and 3. Fmoc-PAL-PEG-resin (0.1 mmol) was swelled in DMF. Then the Fmoc was removed with 20% piperidine in DMF for 20 min. The oligomer was then built up by alternately coupling 10 equivalents of isophthalic acid or diamine **10**. In each case, the couplings were carried out in DMF with 10 equivalents each of 2-(1H-benzotriazole-1-yl)-

Abbreviations: DIEA, diisopropylethylamine; DMF, dimethylformamide; TFA, trifluoroacetic acid; MD, molecular dynamics; MIC, minimal inhibitory concentration.

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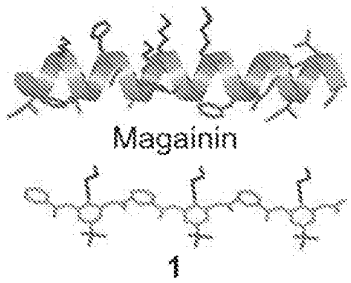


Fig. 1. Amphiphilic structure of 1 and magainin. Hydrophobic side chains are shown in green, and hydrophilic side chains are in blue.

1,1,3,3,-tetramethyluronium hexafluorophosphate (HBTU) and *N*-hydroxybenzotriazole hydrate (HOBt), and 20 equivalents of DIEA for 24 h at room temperature. The oligomers were cleaved from the resin by treatment with TFA/anisole (95:5) for 1 h. Pure oligomers were obtained by HPLC on a reverse-phase C4 column, with a linear gradient from 30% to 80% solvent B in 50 min (solvent A, 0.1% TFA in water; solvent B, acetonitrile/water/TFA 900:99:1). Matrix-assisted laser desorption ionization–time-of-flight MS: **2**: 755.99 (calcd); 756.5 ($M + H^+$); **3**: 1125.47 (calcd); 1125.6 ($M + H^+$).

Antimicrobial Testing. The compounds were dissolved in DMSO/water to make series of stocks of 2-fold dilution and were diluted 10-fold to cell culture on 96-well plates. Minimal inhibitory concentrations (MICs) were obtained by incubating the compounds with the bacteria for 18 h at 37°C and measuring cell growth at OD_{590}.

Vesicle Leakage Assay. The leakage of calcein from large unilamellar vesicles was measured as described (9). The polymer was dissolved in DMSO at concentrations from 300 μg/ml to 37.5 μg/ml. The vesicles were prepared by reverse-phase evaporation in 10 mM sodium phosphate buffer (pH 7) followed by a single extrusion through a 0.2-μm-pore-size polycarbonate filter. The nontrapped calcein was removed by eluting through a size-exclusion Sephadex G-25 column, with 90 mM sodium chloride/10 mM sodium phosphate (pH 7). The leakage process was monitored by following the increase of calcein fluorescence intensity at 515 nm (excitation at 490 nm, slit width 3.8 nm) after 100 μl of polymer stock was added to 1.9 ml of vesicle solution. Complete leakage was achieved by addition of 10 μl of 0.2% Triton X-100 to the 2-ml solution, and the corresponding fluorescence intensity was used as 100% leakage for the calculation of leakage fraction.

Results

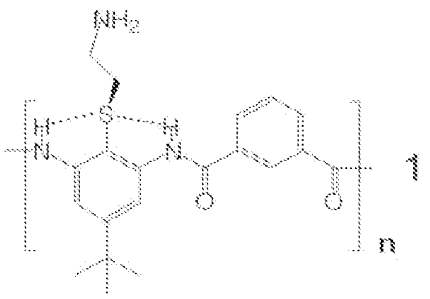
Design. Our initial attempts to design facially amphiphilic structures have focused on AB arylamide polymers typified by **1** (shown below).

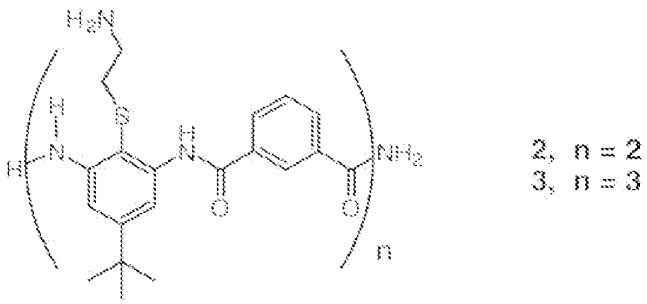
The diamine was chosen for its ease of synthesis and its expected conformational properties. The choice of a thioether was based on the expectation that the methylene bonded to the thioether group would prefer to lie out of the plane of the ring, allowing weak hydrogen bonding to both amide protons. This interaction should stiffen the conformation and help to eliminate the formation of intermolecular hydrogen-bonded aggregates with low solubility.

Computational Studies. Critical to the design of folded polymers is the development of accurate computational methods, analogous to those developed for peptide and protein structures that can predict low-energy conformations of the backbone. Density functional calculations of suitable model compounds were conducted to rigorously determine the torsional barriers for rotation about bonds within the arylamide system. The torsional potential profile (Fig. 2*a*) for a model compound, 2-methylthioacetanilide [$C_6H_4(SCH_3)(NHCOCH_3)$], exemplifies the importance of the designed hydrogen bond on the molecular flexibility of the backbone. [The barrier C C N (H) C(O) height is 8 kJ/mol higher for the CC N(H) C(O), CN(H) C(O) C, N(H)C(O)C C, and C C S C model compound with the methyl-thioether group than for the one without this substituent (Fig. 2*a*), and the overall torsional barrier for the former reaches 63 kJ/mol when the carbonyl O is directed in plane toward S.] Density functional calculations also confirmed that the methylene attached to the thioether sulfur would lie out of the plane of the phenyl ring (data not shown). These torsions were then used together with existing parameters (Fig. 2) to provide an improved molecular mechanics force field for the polymer.

Importantly, model compounds can be synthesized and their structures determined by x-ray diffraction as a test of the new force field. The crystal structure of an appropriate model thioether amide displays the conformational properties expected from the design (Fig. 2*b*). Also, molecular dynamics (MD) simulations of the crystal structure are in excellent agreement with experiment, providing support for the computed torsional potentials (Fig. 2*b*). Encouraged by this agreement, we conducted MD simulations on an oligomer **3** containing six aromatic units in an *n*-octane/water interfacial system. Irrespective of the initial starting configurations, the amphiphilic polyamide rapidly moved to the interface and exposed its polar amine functions into the water phase and its alkyl side chains into the *n*-octane phase (Fig. 2*c*).

Synthesis. Polymers based on the repeat, **1**, are prepared by polycondensation of the diamine with isophthaloyl chloride. The diamine was derived from the commodity chemical 4-*tert*-butylphenol and was synthesized from commercially available 2,6-dinitro-4-*tert*-butyl-phenol and other inexpensive starting materials in several high-yielding steps (>90%) (Scheme 1). Oligomers **2** and **3** (shown below) containing two or three AB units were also prepared by solid-phase methods and purified to homogeneity.





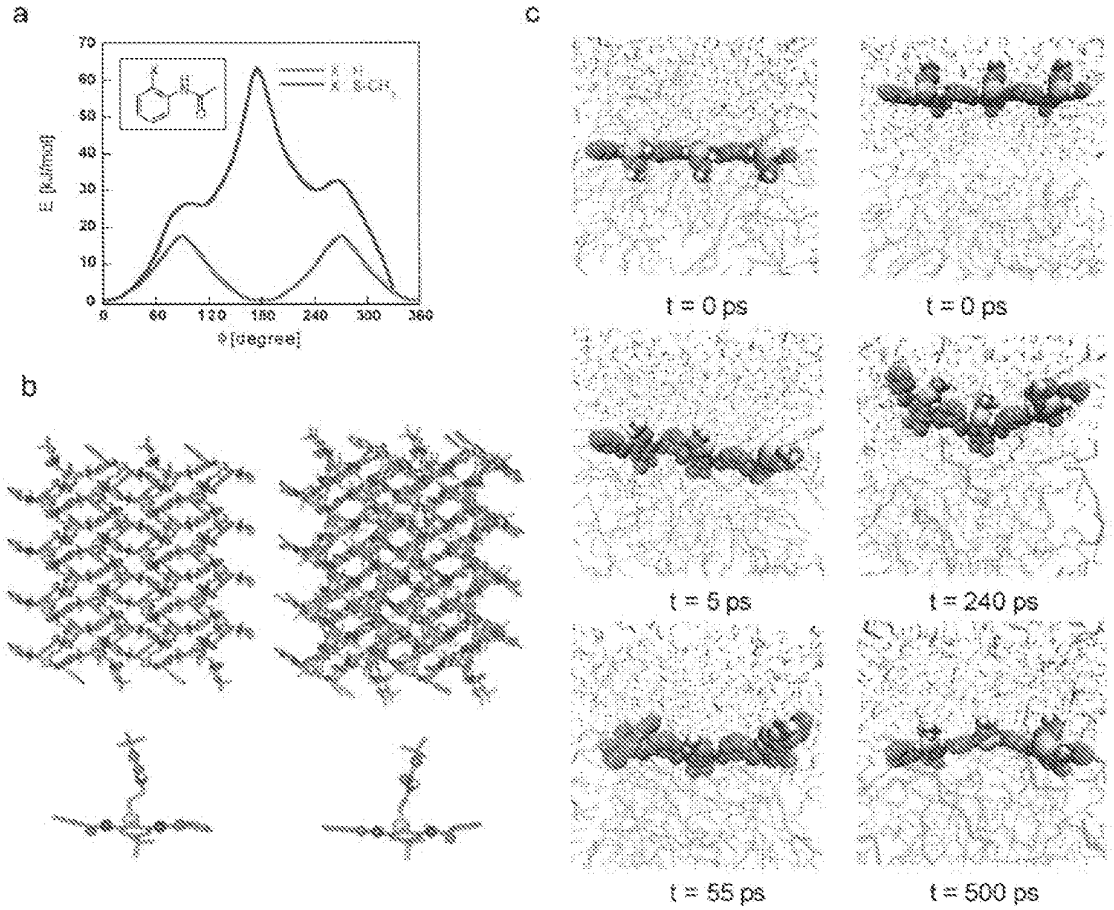


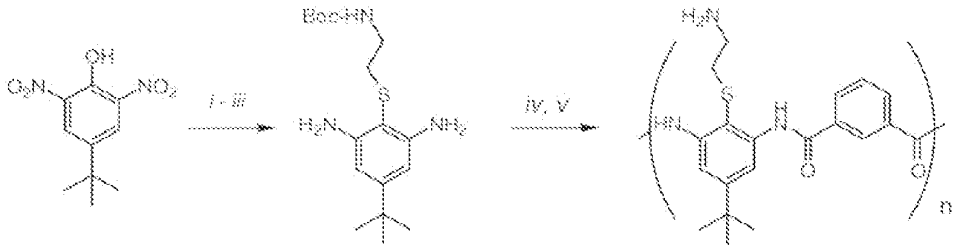
Fig. 2. Computational calculations for aryl amide oligomers. Density functional theory based methods were used to generate torsional potentials, which were then combined with CHARMM (18) bond-stretching and -bending potentials, and TRAPPE (19) and OPLS (20) van der Waals and electrostatic potentials for MD simulations of the designed oligomers. (*a*) Relative energy of different conformations of $C_6H_4(N(H)C(O)CH_3)(X)$, X = H or SCH_3, in which one C-C-N(H)-C(O) torsional angle is held approximately fixed by a Lagrangian multiplier, but all other parameters are relaxed [using the CPMD (19) program with the HCTH (22) density functional]. Zero degrees is defined as the angle that projects the amide proton toward the thioether S. The thioether methyl was initially placed perpendicular to the benzene ring plane, near the minimum conformation for the compound (‖). (*b*) Crystal structure of a model amide. (*Left*) X-ray structure. (*Right*) Simulated structure [from an MD calculation at T = 298 K and *P* = 1 atm (1 atm = 101.3 kPa)]. The top two images are for a 2 × 4 × 2 crystal lattice. Color notation: carbon (green), oxygen (red), nitrogen (blue), polar hydrogen (white), and sulfur (yellow); nonpolar hydrogens are not shown. The x-ray crystal structure vs. calculated results are cell lengths [Å] *a*: 15.34, 14.62; *b*: 8.28, 8.90; *c*: 23.16, 23.23; cell angles [°] α: 90, 90.00; β: 90.78, 94.58; γ: 90, 89.99. (*c*) Snapshots from two sets of MD calculations of oligomer **3** at the *n*-octane/water interface. One started with the entire oligomer immersed in the water phase (*Right*) and the other (*Left*) inside the *n*-octane phase. The initial configurations were generated from a Monte Carlo simulation with configurational-bias Monte Carlo techniques (22–24), and then the dynamic evolution of the polymer was monitored with MD in the isothermal-isobaric ensemble at T = 298 K and *P* = 1 atm. Color notation: *n*-octane (green), water (oxygen: red; hydrogen: white), and chlorine counterion (magenta); oligomer **3** is colored as in *b*.

We also prepared analogous oligoureas by using phenyl 1,3-diisocyanate in place of isophthaloyl chloride. However, these molecules had low aqueous solubility, possibly because of intermolecular hydrogen bond formation involving the additional urea NH groups that are unable to form intramolecular hydrogen bonds.

Antimicrobial Activity. The antimicrobial activity of the arylamides was measured with *Klebsiella pneumoniae* and *Escherichia coli* as Gram-negative strains and *Bacillus subtilis* as a Gram-positive strain (Table 1). Considering the simplicity of their structures, the short oligomers and polymers have good activity when compared with other molecules, including a synthetically modified magainin II derivative [MIC = 3.2 μg/ml vs. *E. coli* JM109 and 1.6 μg/ml vs. *B. subtilis* BR151 (8)] or the antimicrobial cyclic peptides very recently reported by Ghadiri and coworkers (10). There is a trend toward higher activity for the short polymers and oligomers, with an optimal length of ≈8 repeat units in this nonexhaustive survey of activity vs. chain length. The inactivity of the longer polymer may arise from reduced solubility, lower molar concentration (for a given concentration in μg/ml), or inability to penetrate through the proteoglycan layer. Also, acetylation of the highly active polymer with $n = 8$ (Table 1) eliminates the antimicrobial activity, indicating that the positively charged aminoethyl groups are required for activity.

To determine whether the oligomers were bactericidal or bacteriostatic, the *E. coli* were incubated with the polymer ($n = 8$) overnight and then plated in the absence of the polymer. The number of colonies was decreased by at least

‖CPMD/HCTH-isolated molecule calculations were performed in a 10 Å × 12 Å × 12 Å box with valence electron wave functions expanded in plane waves with a 70-Rydberg cutoff and Trouiller–Martins normconserving pseudopotentials.



Scheme 1. (*i*) TsCl, DIEA, CH_2Cl_2; (*ii*) Boc-NH$(CH_2)_2$SH, DIEA, CH_2Cl_2; (*iii*) $SnCl_2$, EtOH 78°C; (*iv*) isophthaloyl chloride, triethylamine, dimethylethylenediamine, DMF; (*v*) TFA.

100-fold relative to that expected from the initial value, indicating that the polymer was acting as a bactericidal agent. One of the hallmarks of the host defense peptides is their activity against a broad spectrum of bacteria (6, 15, 16). The most active polymer was tested against a panel of a number of pathogenic bacteria (Table 2). The MICs were found to be below 50 μg/ml for each of these strains.

To confirm that the polymers and oligomers are indeed able to interact with and disrupt phospholipid bilayers, we measured the ability of **2** to induce leakage of a dye, calcein, entrapped within the interiors of large unilamellar vesicles of mixed phosphatidylserine and phosphatidylcholine lipids (SOPS/SOPC 1:9). The extent of leakage of encapsulated calcein was detected by its fluorescence at 515 nm (Fig. 3). Oligomer **2** gave rise to calcein leakage in a dose-dependent manner. As was observed for antimicrobial peptides (9), the value of IC_{50} for this assay was approximately 10-fold lower than the MIC values for the *E. coli*.

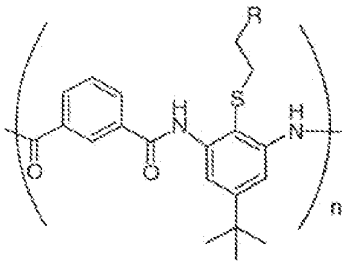
Conclusions

Here we describe a class of *facially amphiphilic* polymers, in which hydrophobic and hydrophilic groups segregate onto opposite sides of a low-energy, repeating conformation (secondary structure). Amphiphilic polymers have many applications in colloid and surface science but they are generally formed by random copolymerization of hydrophobic and hydrophilic monomers, or by combining a hydrophilic block with a hydrophobic block to provide a detergent-like structure. Indeed, many amphiphilic block polymers form micellar and bilayer phases. By contrast, the facially amphiphilic polymers described in this work should be able to mimic a variety of surface-active peptides and proteins. By varying the charge and hydrophobicity of the side chains one might be able to mimic the properties of toxins such as melittin, selective antimicrobials, or apolipoproteins, all of which have been successfully mimicked by using β-peptides of defined length and sequence (7–9, 13). Thus, although compounds 2–5 show hemolytic activity, we expect this feature can be eliminated in subsequent rounds of design.

By preparing both oligomers of defined length as well as the corresponding polymers, one can combine the advantages of studying both classes of compounds. Defined oligomers are homogeneous organic compounds that are useful for structural studies, thermodynamic analyses, and provide well defined structure-activity relationships. However, polymers are easy to prepare in large quantities and are the products of choice for applications in which the cost of production is an issue.

In summary, this study provides a one-pot synthetic strategy to produce polymers with a specified facially amphiphilic

Table 1. Antibacterial activities of polyamides

Oligomer		n	R	MIC, μg/ml[§] *E. coli*	*K. pneumoniae*[‡]	*B. subtilis*[¶]
	**2**	2	NH_3^+	19	66	12
	3	3	NH_3^+	<19	NA	19
	4	8*†	NH_3^+	7.5–15	31–50	16
	5	60*	NH_3^+	>200	----	----
	6	8*†	NH-Ac	>500	250	>500

*The average chain length is determined by the Flory equation, and the polymeric nature of the products is confirmed by gel permeation chromatography with methods similar to those described earlier (11). Polydispersity index: 1.10 (**4**), 1.64 (**5**).

†The end groups were *N,N*-dimethylethylenediamine amides obtained by using *N,N*-dimethylethylenediamine as a terminator.

‡Mueller–Hinton medium.

§MICs were obtained by incubating 2-fold dilution series of polymers with the bacteria for 18 h at 37 °C and measuring cell growth at OD_{590}.

¶LB medium.

Table 2. Activity of 4 against six different bacterial strains

Strain	MIC, μg/ml[§]
E. coli K91	12–50[¶]
E. coli D31*	7.5–15[‖]
K. pneumoniae 10	31–50[‖]
Salmonella typhimunium 55[†]	<3.75**
Pseudomonas aeruginosa 10	31–62[‖]
Enterococcus faecium[‡]	15–25[††]

*Ampicillin- and streptomycin-resistant.
[†]Tetracycline-resistant.
[‡]Gram-positive.
[§]Minimal inhibitory concentration at 18 h.
[¶]Minimal medium.
[‖]Quarter strength Mueller–Hinton (MH) medium.
**Half strength MH medium.
[††]Quarter strength Bushnell–Hass medium.

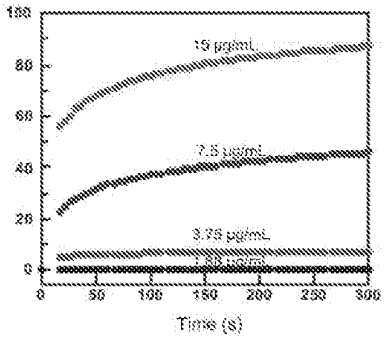


Fig. 3. Calcein efflux induced by oligomer **2**. Fraction of leakage was calculated from the fluorescence intensity at 515 nm, with 100% leakage calibrated by addition of 0.2% Triton X-100.

secondary structure and broad antibacterial activity. These polymers differ from earlier dendrimeric and cationic antimicrobial polymers (14, 17) in that they mimic the essential features of a large class of antimicrobial peptides and proteins. By systematically varying the side chains and possibly also the polymeric backbone it should be possible to fine-tune the antimicrobial selectivity and toxicity of the polymers in a manner analogous to antimicrobial peptides and β-oligomers (7, 9).

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Exhibit 11

US007173102B2

(12) **United States Patent**
DeGrado et al.

(10) **Patent No.: US 7,173,102 B2**
(45) **Date of Patent: Feb. 6, 2007**

(54) **FACIALLY AMPHIPHILIC POLYMERS AS ANTI-INFECTIVE AGENTS**

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C08G 63/00	(2006.01)
C08G 69/02	(2006.01)
C08G 71/02	(2006.01)

(52) **U.S. Cl.** **528/322**; 528/310; 528/190; 528/191; 528/192; 528/193; 528/272; 528/327; 428/59; 428/123; 428/357; 428/409; 428/543; 428/152, 428/153; 424/76.8; 424/78.08; 424/401; 424/402; 424/422; 424/423; 424/424; 424/443; 427/256

(58) **Field of Classification Search** 528/322, 528/310, 190–193, 272, 44–45, 49, 327; 606/228; 428/59, 123, 152–153, 357, 409, 428/543; 424/76.8, 78.04, 401–402, 405, 424/422–424, 443; 604/358, 374, 360, 372; 427/256

See application file for complete search history.

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(74) *Attorney, Agent, or Firm*—Sterne, Kessler, Goldstein & Fox P.L.L.C.

(57) **ABSTRACT**

Facially amphiphilic polymers and articles made therefrom having biocidal surfaces are disclosed. The polymers can inhibit the growth of microorganisms in contact with the surface or in areas adjacent to said biocidal surface. There is also disclosed a method to identify and optimize the facial amphiphilicity of polyamide, polyester, polyurea, polyurethane, polycarbonate and polyphenylene polymers. Utility as a contact disinfectant is disclosed.

45 Claims, 11 Drawing Sheets

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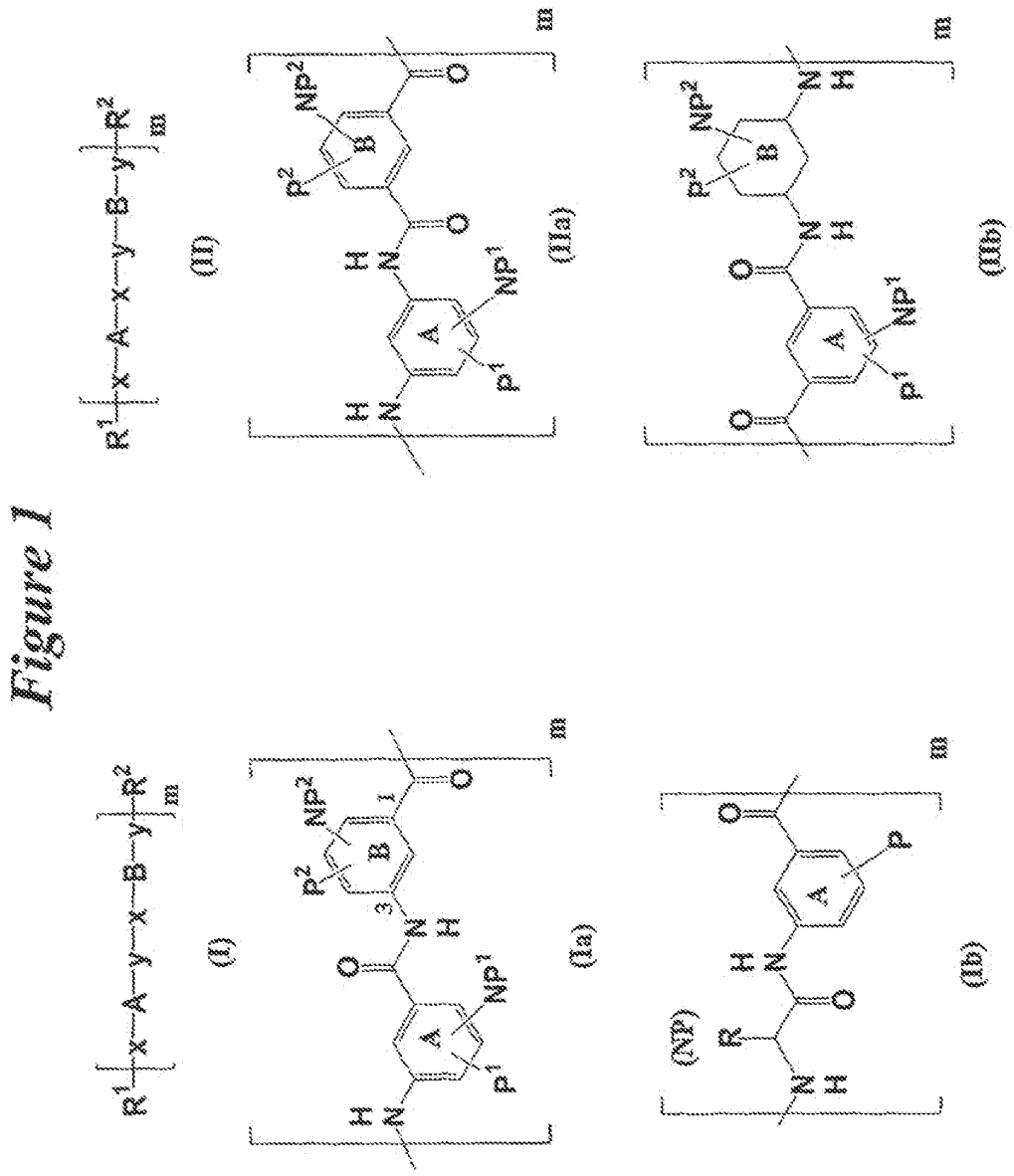
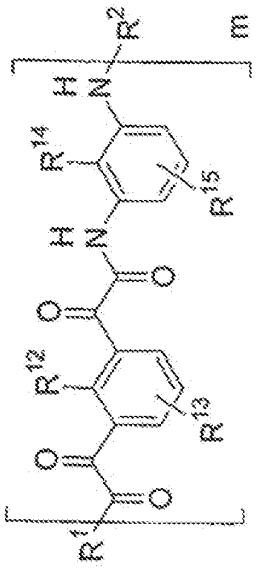
Figure 1





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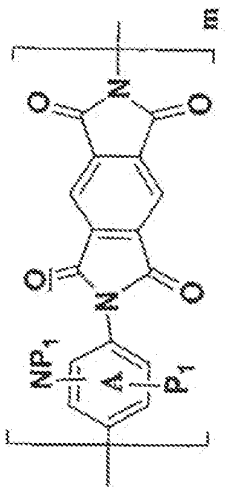

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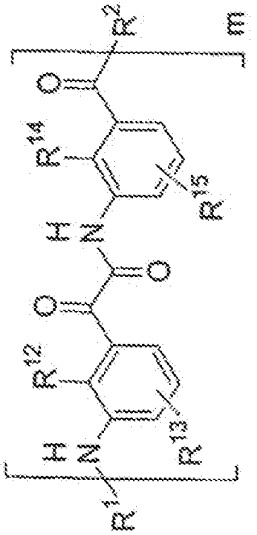

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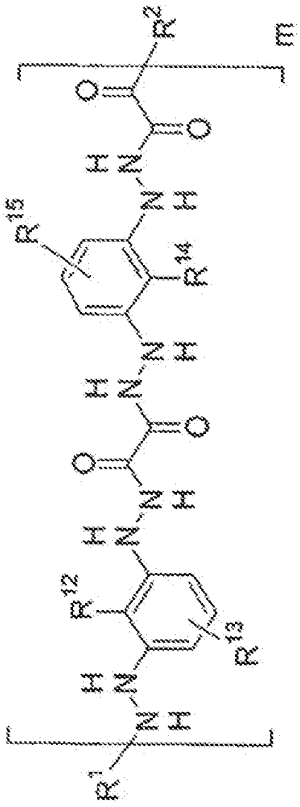


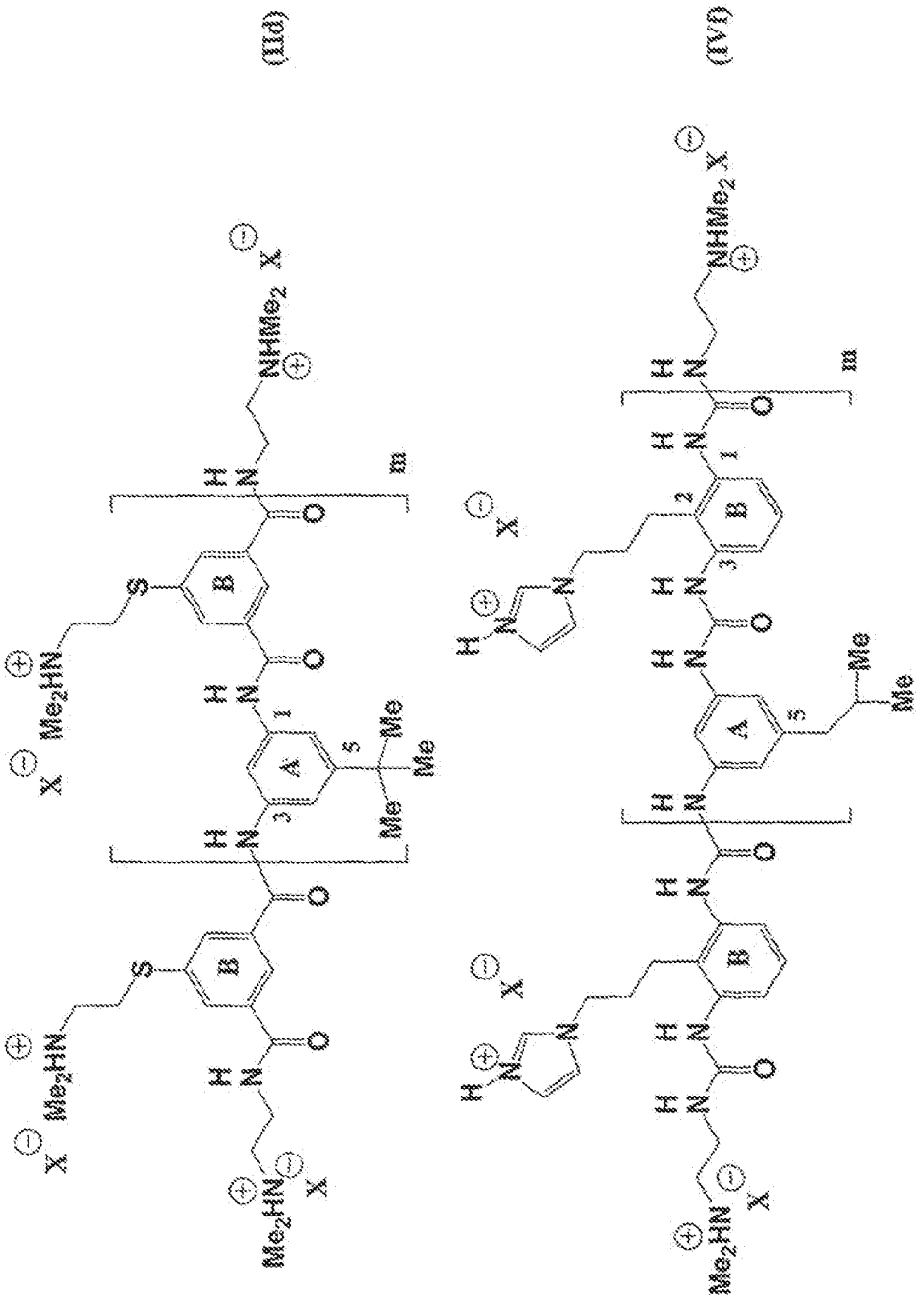
(XVII)

Figure 2

Figure 3

P	NP'	R
O-CH_2-CH_2-NMe_2	O-CH_2CH_3	O-CH_2-CH_2-CH_3
O-CH_2-CH_2 –(2-pyridyl)	O-CH_2CHMe_2	O-$CH_2CH_2CH(CH_3)_2$
O-CH_2-CH_2-$N(CH_2$-CH_2-$NMe_2)_2$	O-$CHMe_2$	O-$CH_2CH_2CH_2CH_3$
O-CH_2-CH_2 –(2-imidazolyl)	OCMe_3	O-CH_2-CH_3
O-CH_2-CH_2-NH-$C(=NH)NH_2$	O-CH_2-$CHMe_2$	O-CH_2-CH_2-CH_3
O-CH_2-CH_2-$N(CH_2CH_3)_2$NH	O$(CH_2)_4Me$	O-$CH_2CH_2CH_2CH_3$

Figure 4



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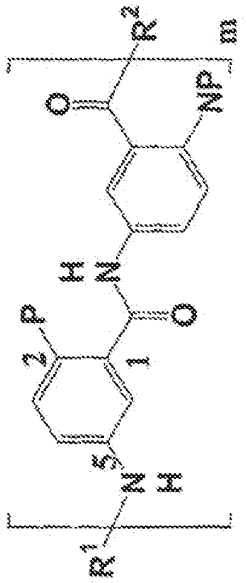

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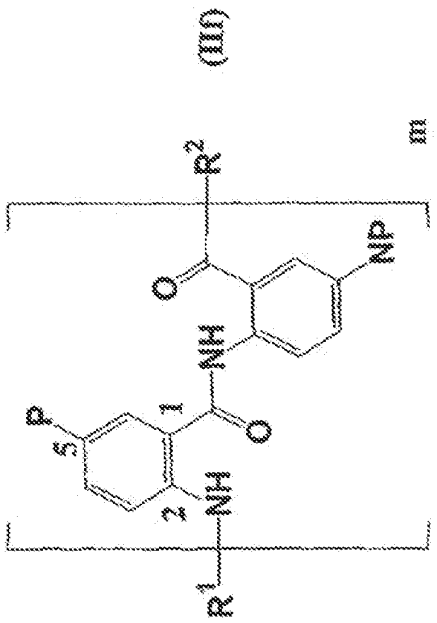


(IIf)

P	NP'
O-CH_2-CH_2 NMe_2	O-CH_2CH_3
O-CH_2-CH_2 –(2-pyridyl)	O-CH_2CHMe_2
O-CH_2-CH_2 $N(CH_2$-CH_2-$NMe_2)_2$	O-$CHMe_2$
O-CH_2-CH_2 –(2-imidazolyl)	OCMe_3
O-CH_2-CH_2 NH-C(=NH)NH_2	O-CH_2-$CHMe_2$
O-CH_2-CH_2 $N(CH_2CH_2)_2NH$	O$(CH_2)_4Me$

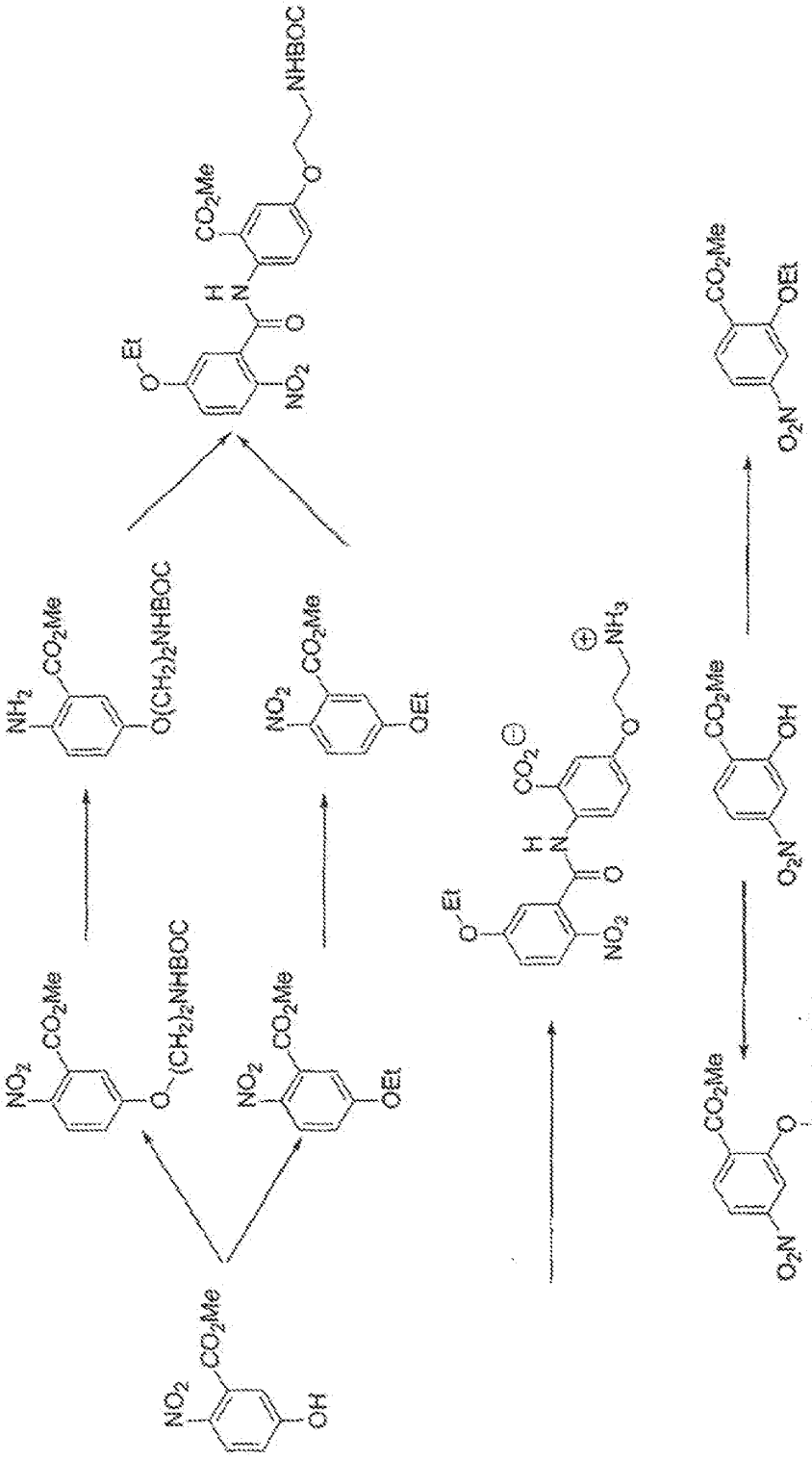
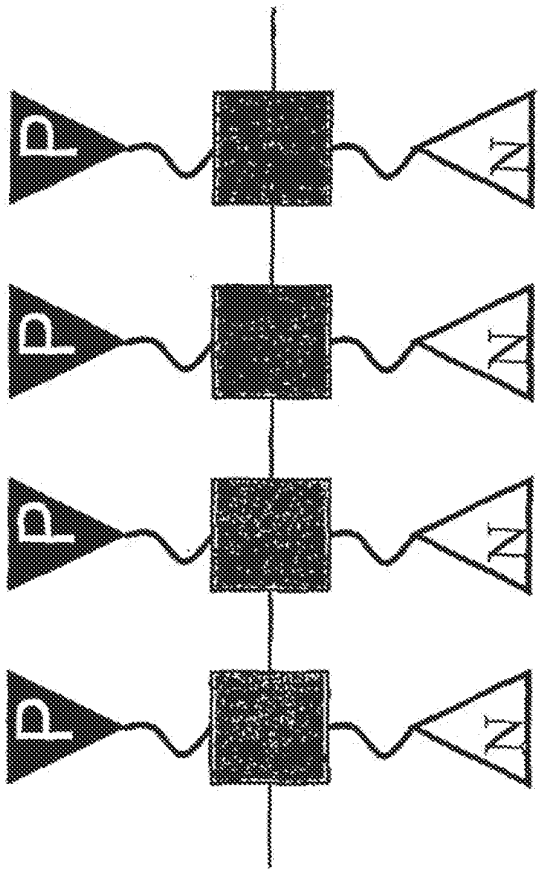
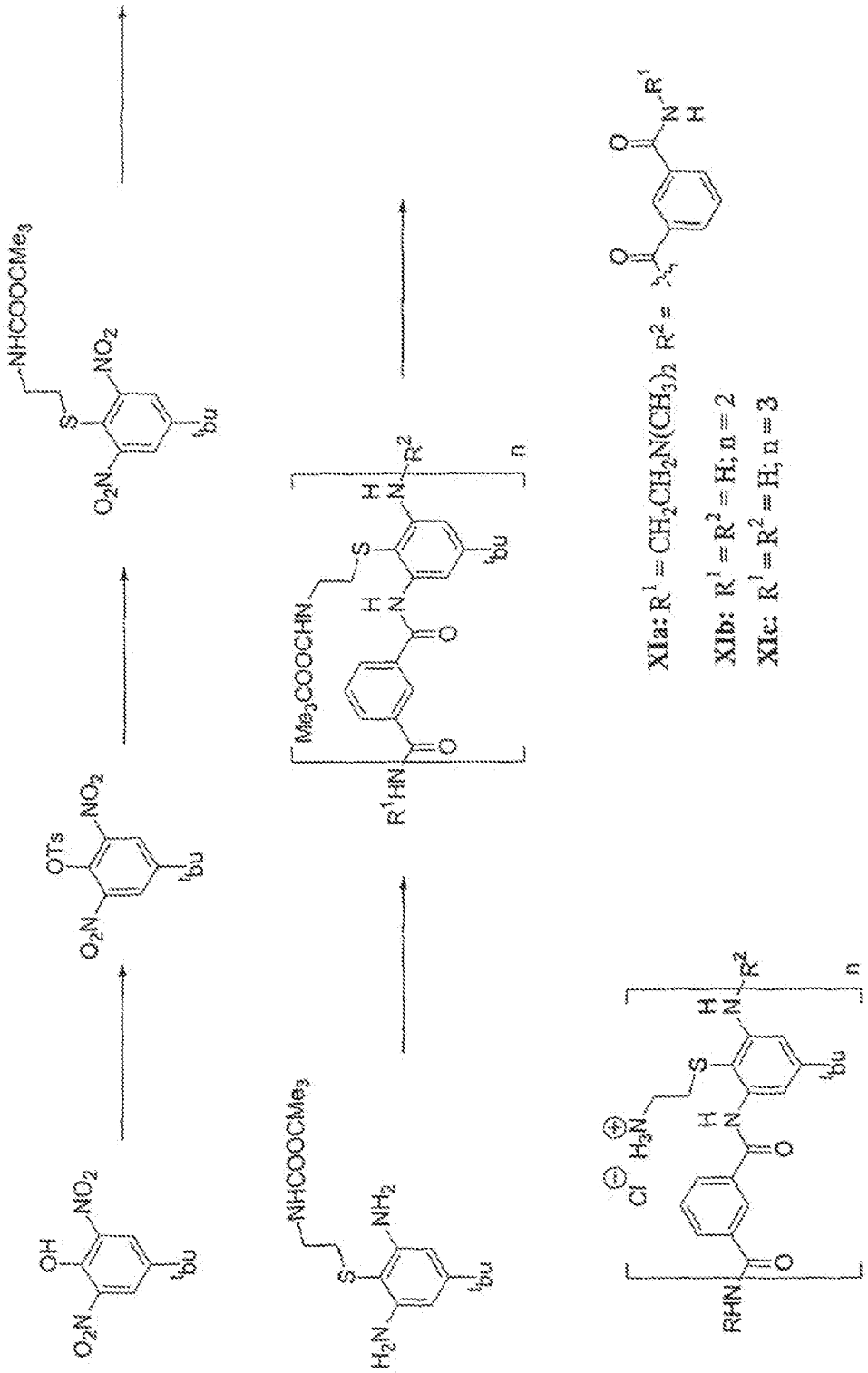


Figure 6

Figure 7



P = polar group N = nonpolar group

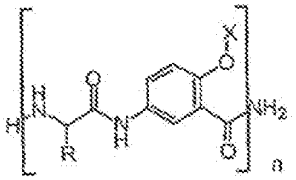


XIa: $R^1 = CH_2CH_2N(CH_3)_2$ $R^2 =$

XIb: $R^1 = R^2 = H$; n = 2

XIc: $R^1 = R^2 = H$; n = 3

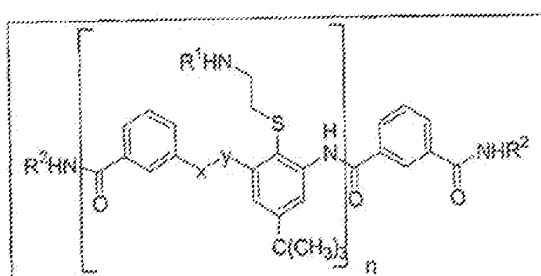
Figure 8



			Antimicrobial Activity MIC (μg/mL)[1]			Hemolytic Activity HC_{50} (μg/mL)
R	X	n	*E. c.*	*K. p.*	*B. s.*	
$CH_3CH(CH_3)_2$	$(CH_2)_3NHC(=NH)NH_2$	4	20	50	6	200
		5	20	25	6	200
	$(CH_2)_3NH_2$	4	12	50	6	200
		5	12	50	6	200
	$(CH_2)_3NHC(=NH)NH_2$	4	12	50	12	35
		5	12	50	12	8
	$(CH_2)_3NH_2$	2	>60	500	8	>200
		3	>500	>500	37	>200
		4	~30	63	8	>200
$CH(CH_3)_2$	$(CH_2)_3NH_2$	4	100	500	100	
		5	100	500	100	
$CH(CH_3)CH_2CH_3$	$(CH_2)_3NH_2$	4	500	500	20	
		5	100	500	20	
C_6H_5	$(CH_2)_3NH_2$	4	500	500	100	
		5	500	>500	100	
n-C_4H_9	$(CH_2)_3NH_2$	4	500	500	500	
		5	100	500	100	
$(CH_2)_3NHC(=NH)NH_2$	Me	4	>500	500	500	
		5	500	500	500	
$(CH_2)_3NHC(=NH)NH_2$	*iso*-pentyl	4	100	100	6	4
		5	100	100	12	4
$(CH_2)_4NH_2$		2	>500	>500	25	
		4	63	63	<5	

[1] E.c. *Escherichia coli* D31; K.p. *Klebsiella pneumoniae* 10; B.s. *Bacillus subtilis*

Figure 9

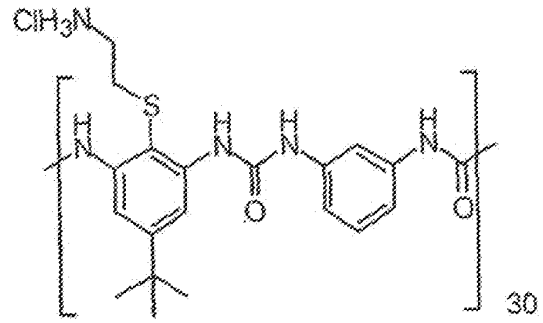


$R^2 = CH_2CH_2N(CH_3)_2$

				Antimicrobial Activity MIC (μg/mL)					
-x-y-	R^1	n	M_p[7]	K91[1]	K91[2]	D31[3]	K.p.[4]	B.s.[5]	rbc[6]
-CONH-	H	2	756[8]		<18	19	66	12	50
	H	3	1125[8]		<19		19		20
	H	10	6000[9]	<25	12-50	7.5-15	31-50		1
	H	>30	20,000	>200					5
	$C(=NH)NH_2$		6000			25	100	12.5	8
-NHCONH-	H	2	745[8]	<12.5					15
	H	10	6000		<50				5
	H	>30	20000		100				20

[1] *E. coli* K91 (M9 medium)
[2] *E. coli* K91 (LB medium)
[3] *E. coli* D31 (MH medium)
[4] *Klebsiella pneumoniae* 10 (MH medium)
[5] *Bacteria subtilis* (LB medium)
[6] hemolytic activity-erythrocytes HC_{50} (μg/mL)
[7] The average chain length is determined by the Flory equation and the polymer size is confirmed by gel chromatography with Waters styryl-gel columns were connected in series to give a MW range from 1,000,000 to 300 The peak was eluted with THF and the peak center at maximum height using a size exclusion column. Average polydispersity for these condensation polymers is ~2.5.
[8] Homogenous compound prepared by solid phase synthesis.
[9] *Pseudomonas aeruginosa* 10 IC_{50} 31-62; *Salmonella typhimurium*, S5 IC_{50} <3.75; *Enterococcus faecium* IC_{50} 15-25 (μg/mL).

Figure 10



MIC = 25 μg/ml polyurea
MIC = 5 μg/ml magainin

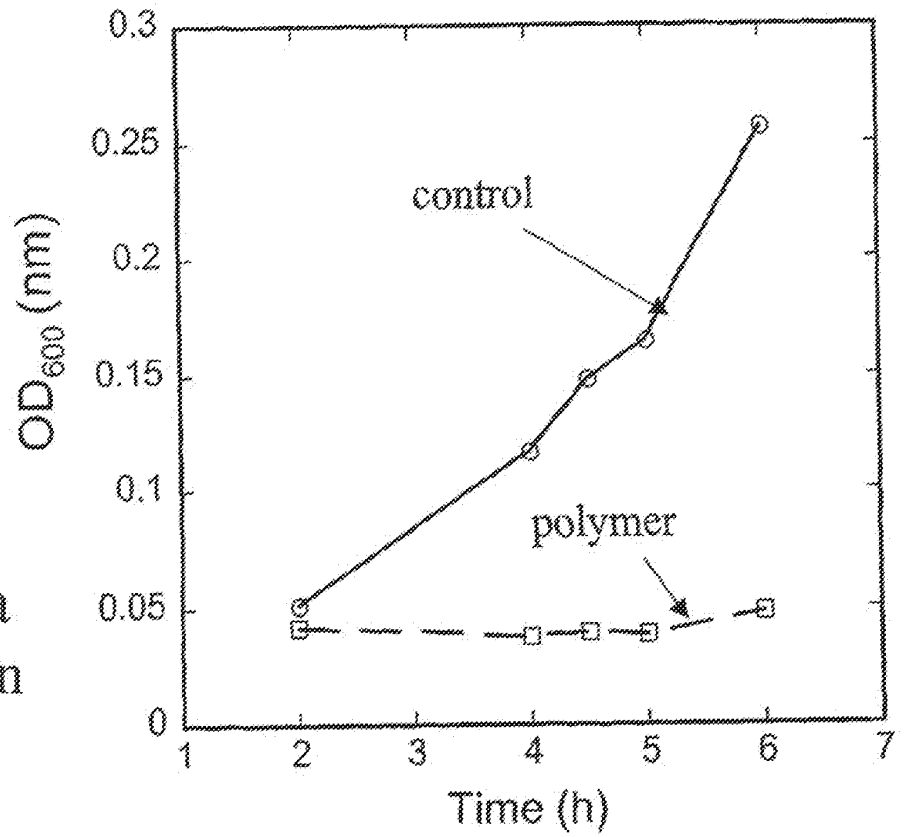


Figure 11

FACIALLY AMPHIPHILIC POLYMERS AS ANTI-INFECTIVE AGENTS

REFERENCE TO PREVIOUS APPLICATIONS

This application claims priority to U.S. Provisional Patent Application Ser. No. 60/274,145 filed Mar. 8, 2001.

GOVERNMENT SUPPORT

This invention was supported in part by funding from the U.S. Government (NSF Grant DMR00-79909) and the U.S. Government may therefore have certain rights in the invention.

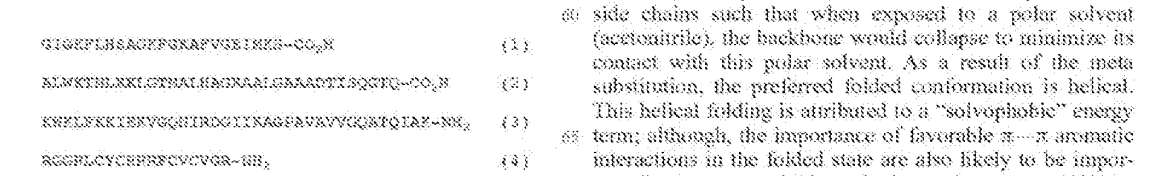
FIELD OF THE INVENTION

The present invention relates to the design and synthesis of facially amphiphilic polymeric compounds with microbiocidal properties that can be coated on or incorporated into materials and methods to design the same. The present invention further relates to methods to identify and design facially amphiphilic polymers and methods to prevent or limit microbial growth.

BACKGROUND OF THE INVENTION

Amphiphilic molecules exhibit distinct regions of polar and nonpolar character. These regions can result from substitution of hydrophobic and hydrophilic substituents into specific and distinct regions of conformationally defined molecules. Alternately a conformationally flexible molecule or macromolecule can adopt an ordered structure in which the hydrophobic and hydrophilic substituents on the molecule segregate to different areas or faces of the molecule. Commonly occurring amphiphilic molecules include surfactants, soaps, detergents, peptides, proteins and copolymers. These molecules have the capacity to self-assemble in appropriate solvents or at interfaces to form a variety of amphiphilic structures. The size and shape of these structures varies with the specific composition of the amphiphilic molecule and solvent conditions such as pH, ionic strength and temperature.

Amphiphilic peptides with unique broad-spectrum antimicrobial properties have been isolated from a variety of natural sources including plants, frogs, moths, silk worms, pigs and humans (H. G. Boman *Immunol Rev.* 2000 173: 5–16; R. E. Hancock and R. Lehrer, *Trends Biotechnol.* 1998 16:82–88). These compounds include the magainin I (1) and dermaseptin S1 (2) isolated from the skin of frogs and the cecropin A (3) isolated from the *cecropia* moth. These naturally occurring compounds have broad-spectrum antibacterial activity and they do not appear prone to the development of bacterial resistance. These compounds are relatively low molecular weight peptides that have a propensity to adopt α-helical conformation in hydrophobic media or near a hydrophobic surface and as a result are facially amphiphilic (i.e., one-third to two-thirds of the cylinder generated by the helical peptide has hydrophobic side chains while the



remainder has hydrophilic side chains. These hydrophilic side chains are primarily positively-charged at neutral pH. Hydrophobic amino acids compose 40–60% of the total number of residues in most anti-microbial peptides. The selectivity of the amphiphilic peptides (e.g. for bacteria vs. human erythrocytes) depends on the overall hydrophobicity. The biological activity of thee compounds depend on the ratio of charged (c) to hydrophobic (h) residues. When the ratio is varied from 1:1 (c:h) to 1:2 (c:h) peptides with more hydrophobic residues tend to be more active toward erythrocyte membranes. The physiochemical properties rather than the presence of particular amino acids or the tertiary structure of the side chains. Related peptides have been isolated from mammals and these anti-microbial peptides have been suggested to be an important component of the innate immune response. (Gennaro, R. et al. *Biopolymers* (*Peptide Science*) 2000, 55, 31).

These observations recently have been extended to peptides (β-peptides) comprised of β-amino acids. These non-natural polypeptide mimetics also are capable of adopting stable α-helical and β-sheet structures although the precise geometries of these structure are different form those generated by α-amino acid oligomers. However, appropriate positioning of hydrophobic and hydrophilic residues results in amphiphilic conformations with similar antimicrobial properties. This further confirms the importance of repeating periodicity of hydrophobic and hydrophilic groups vis-à-vis the precise amino acid sequence in producing facial amphiphilic antimicrobial compounds. (D. Seebach and J. L. Matthews, *Chem Commun.* 1997 2105; Hamuro, Y., Schneider, J. P., DeGrado, W. F., *J. Am. Chem. Soc.* 1999, 121, 12200–12201; D. H. Appella et al., *J. Am. Chem. Soc.*, 1999 121, 2309).

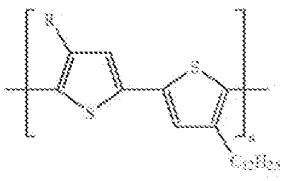
Secondary structures other than helices may also give rise to amphiphilic compounds. The protegrins (4) are a related series of anti-microbial peptides. (J. Chen et al., *Biopolymers* (*Peptide Science*), 2000 55 88) The presence of a pair of disulfide bonds between Cys^6–Cys^{15} and Cys^8–Cys^{13} results in a monomeric amphiphilic anti-parallel β-sheet formed by the chain termini and linked by a β-turn. The amphiphilic β-sheet conformation is essential for anti-microbial activity against both gram-positive and gram-negative bacteria.

The data related to anti-microbial peptides suggests that facial amphiphilicity, the alignment of polar (hydrophilic) and nonpolar (hydrophobic) side chains on opposite faces of a secondary structural element formed by the peptide backbone, and not amino acid sequence, any particular secondary/tertiary structure, chirality or receptor specificity is responsible for their biological activity.

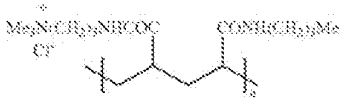
Suitably substituted polymers which lack polyamide linkages also are capable of adopting amphiphilic conformations. Solid phase chemistry technology was utilized to synthesize a class of meta substituted phenylacetylenes that fold into helical structures in appropriate solvents (J. C. Nelson et al., *Science* 1997 277:1793–96; R. B. Prince et al., *Angew. Chem. Int. Ed.* 2000 39:228–231). These molecules contain an all hydrocarbon backbone with ethylene oxide side chains such that when exposed to a polar solvent (acetonitrile), the backbone would collapse to minimize its contact with this polar solvent. As a result of the meta substitution, the preferred folded conformation is helical. This helical folding is attributed to a "solvophobic" energy term; although, the importance of favorable π—π aromatic interactions in the folded state are also likely to be important. Furthermore, addition of a less polar solvent ($CHCl_3$)

results in an unfolding of the helical structure demonstrating that this folding is reversible.

Regioregular polythiophenes (5 and 6) have been shown to adopt amphiphilic conformations in highly ordered π-stacked arrays with hydrophobic side chains on one side of the array and hydrophilic side chains on the other side. These polymers form thin films useful in the construction of nanocircuits. (Bjornholm et al., *J. Am. Chem. Soc.*, 1998 120, 7643) These materials would be facially amphiphilic as defined herein; however, no biological properties have reported for these compounds.



5: R = $CH_2CO_2^-NMe_4^+$
6: R = $(CH_2CH_2O)_3Me$



Antimicrobial peptides have been incorporated onto surfaces or bulk materials, with some retention of antimicrobial properties. Haynie and co-workers at DuPont have investigated the activity of Antibacterial peptides have been covalently attached to solid surfaces (S. L. Haynie et al., *Antimicrob Agents Chemother.* 1995 39:301–7; S. Margel et al., *J Biomed Mater Res.* 1993, 27:1463–76). A variety of natural and de novo designed peptides were synthesized and tested for activity while still attached to the solid support. The activity of the peptides decreased when attached to the solid support although the peptides retained their broad spectrum of activity. For example, a de novo designed peptide referred to as E14LKK has a MBC (minimum bactericidal activity) of 31 μg/ml in solution as opposed to 1.5 mg/ml when attached to a solid phase bead. The peptides were attached to the resin with a 2 to 6-carbon alkyl linker. The porosity of Pepsyn K, the resin used in the synthesis, is small (0.1 to 0.2 μm) compared to the bacteria, so the microbes may be unable to penetrate into the interior of the resin. Thus the great majority of the peptide would not be available for binding to cells. The antimicrobial activity did not arise from a soluble component; no leached or hydrolyzed peptide was observed and the soluble extracts were inactive. These studies indicate quite convincingly that antimicrobial peptides retain their activity even when attached to a solid support. However, there is a need to optimize the presentation of the peptides to increase their potency.

Other antimicrobial polymeric materials have been reported which contain chemical functionality known to be antimicrobial (J. C. Tiller et al., *Proc Natl Acad Sci U S A.* 2001 98:5981–85). A large portion of this work uses chemical functions such as alkylated pyridinium derivatives, which are known to be toxic to mammalian cells. The antibiotic ciprofloxacin has been grafted into a degradable polymer backbone (G. L. Y. Woo, et al., Biomaterials 2000 21:1235–1246). The activity of this material relies on cleavage of the active component from the polymer backbone.

Anti-infective vinyl copolymers, wherein monomers with hydrophobic and hydrophilic side chains have been randomly polymerized to produce polymers with amphiphilic properties, have also been described recently W. H. Mandeville III et al. (U.S. Pat. No. 6,034,129). These materials are produced by polymerization of hydrophobic and hydrophilic acrylate monomers. Alternately, the hydrophobic side chain is derived from a styrene derivative which is copolymerized with a hydrophilic acrylate monomer wherein an ionic group is linked to the carboxylic acid. These polymers, however, have relatively random arrangements of polar and nonpolar groups and are not facially amphiphilic as defined herein.

An alternative method to make amphiphilic polymers is to produce block copolymers comprised of hydrophobic blocks (A) and hydrophilic blocks (B), commonly polypropyleneoxy and polyethyleneoxy segments respectively, into A-B, A-B-A or similar copolymers. These copolymers also are not facially amphiphilic as defined herein.

BRIEF DESCRIPTION OF FIGURES

BRIEF DESCRIPTION OF THE DRAWINGS

Specific embodiments of the invention have been chosen for the purpose of illustration and description but are not intended in any way to restrict the scope of the invention. These embodiments are shown in the accompanying drawings wherein:

In FIG. **1** there is shown a cartoon that depicts the separation of hydrophobic and hydrophilic side chains onto opposite faces of the polymer backbone.

In FIG. **2** there is shown the general structure of a facially amphiphilic polyamide or polyester copolymer formulae I and II, representative monomer units for aromatic polyamides, Ia and IIa, the two representative monomer units for polyamides with both aromatic and aliphatic components, Ib and IIb.

In FIG. **3** there is shown the general structure of polyamides with extended linking groups between the monomers.

In FIG. **4** there is shown the general structure IV of a facially amphiphilic polyurea, polycarbonate and polyurethane copolymers and representative monomer units IVa, IVb and IVc, respectively. Examples of two typical polyurea monomers are exemplified in IVd and IVe.

In FIG. **5** there is shown the complete structure of a facially amphiphilic polyamide IId and polyurethane IVf.

In FIG. **6** there is shown typical examples of ortho- and meta-phenylene facially amphiphilic polymers XII and XIII respectively derived from salicylamide and anthranilamide.

In FIG. **7** there is shown the synthesis of substituted salicylic and anthranilic acid monomers of XII and XIII.

In FIG. **8** there is shown the synthesis of polyureas XIa–XIc.

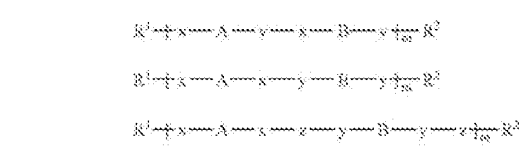
In FIG. **9** there is shown antimicrobial data for polyamide and polyurea oligomers

In FIG. **10** there is shown antimicrobial data for polyamide oligomers of general formula VII.

In FIG. **11** there is shown the time course for antibacterial activity of a polyurea oligomer.

SUMMARY OF THE INVENTION

One object of the invention is to provide new polymeric compounds with anti-microbial properties which can be applied to or dispersed throughout devices, articles and surfaces and which are capable of killing microorganisms on contact, but leach into the environment more slowly than traditional small molecule anti-microbials. The polymeric materials may be deposited as a film on the surface of a substrate or may be dispersed



throughout a substrate to provide an anti-microbial surface. The polymeric materials of the present invention are anti-microbial polymers that are designed to possess amphiphilic properties in the presence of microbial cell walls and to disrupt the membrane and kill the organism. The polymeric materials are further designed to have low toxicity to mammalian cells.

The facially amphiphilic polymers of the present invention are polyamide or polyester compounds of formulae I and II wherein x is O, NR^5 or S, y is CO, CS or SO_2 and A and B are aromatic, heteroaromatic or aliphatic moieties appropriately substituted with polar and nonpolar groups; polyurea, polycarbamate, or polycarbonates compounds of formulae IV wherein x and y are O, NR^5 or S, z is CO, CS or SO_2 and A and B are aromatic, heteroaromatic or aliphatic moieties appropriately substituted with polar and nonpolar groups; and polyphenylene and heteroarylene compounds of formula V wherein is either a single bond, double bond, triple bond or absent and A and B are aromatic, heteroaromatic moieties appropriately substituted with polar and nonpolar groups. R, R^1 and R^2 are end groups appropriate for the specific polymer chain and their design is well know in the polymer art.

These facially amphiphilic polymers are capable of adopting repeating secondary structural motifs that allow for the segregation of polar and nonpolar regions of the molecule into different spatial regions. The anti-microbial polymers adopt amphiphilic conformations when placed in contact with the cell walls of microorganisms and the amphiphilic molecules are capable of disrupting essential cell wall functions resulting in the death of the microorganism.

The present invention further provides methods for killing microorganism on surfaces by disposing thereon a facially amphiphilic polymer. The method for making compositions incorporating the facially amphiphilic polymers includes providing a solution dispersion or suspension of the polymer and applying it to the surface. Alternately compositions can be prepared by incorporating the polymer into plastics that subsequently are molded, shaped or extruded into other articles. The optimal method to deliver the polymer will depend on several factors including the desired coating thickness and the nature and configuration of the substrate and the physical characteristics of the facially amphiphilic polymer.

The facially amphiphilic polymers of the present invention can have a substantial range in molecular weight. Facially amphiphilic molecules with molecular weights of about 0.8 kD to about 20 kD will be more prone to leach from the surface of the substrate. The facially amphiphilic polymer may be attached or immobilized on the substrate by any appropriate method including covalent bonding, ionic interaction, coulombic interaction, hydrogen bonding or cross-linking. The polymers of the present invention provide a surface-mediated microbiocide that only kills organisms in contact with the surface. Moreover the polymers of the present invention are stable and retain their bioactivity for extended periods of time and are nontoxic to birds, fish, mammals and other higher organisms.

The present invention further provides a computational technique to evaluate the energy of polymer conformations and identify polymers which have the capability of exhibiting amphiphilic behavior and aid in identifying optimal sites for substitution of polar and nonpolar substituents that confer amphiphilic properties.

DETAILED DESCRIPTION OF THE INVENTION

Microbial infections represent a serious continuing problem in human and animal health. While amphiphilic α and β-peptides exhibit potent antibacterial, they are, nevertheless, difficult and expensive to prepare in large quantities. Peptides are sensitive to enzymatic and chemical hydrolysis. Exposure to microbial pathogens can occur in a variety of ways. Most objects encountered daily have the potential for harboring infectious organisms and new compounds and approaches for controlling the growth of microbes are extremely valuable and have significant commercial potential. Antimicrobial peptides related to the magainins have desirable biological activities but their utility is limited. An object the present invention is to provide new stable anti-microbial polymers which are available from inexpensive and readily available monomers and which can be incorporated into, or on to, a wide variety of materials and can withstand chemical and enzymatic degradation.

In recent years, the design of non-biological polymers with well-defined secondary and tertiary structures (S. H. Gellman et al., *Acc. Chem. Res.* 1998 31:173–80; A. E. Barron and R. N. Zuckerman, *Curr. Opin. Chem. Biol.*, 1999 3:681–687; K. D. Stigers et al., *Curr. Opin. Chem. Biol.*, 1999 3:714–723) has become an active area of research. One reason for this interest is that for the first time, modern methods of solid phase organic chemistry (E. Atherton and R. C. Sheppard, *Solid Phase Peptide Synthesis A Practical Approach* IRL Press Oxford 1989) have allowed the synthesis of homodisperse, sequence-specific oligomers with molecular weights approaching 5,000 Daltons. The development of this new field of homodisperse sequence-specific oligomers promises to generate molecules with novel chemical and physical properties that will span the gap between polymer and protein science. Polymers are statistical mixtures of molecules typically composed of one to a few monomers. By contrast, peptides and proteins are molecules typically composed from >15 monomers with exact control over sequence, topology, and stereochemistry. These homodisperse sequence-specific oligomers represent molecules with features of both polymers and proteins.

Facially amphiphilic polymers can be homopolymers wherein one monomer is substituted with both a nonpolar and a polar substituent or copolymers wherein one monomer is substituted with a polar substituent and the other monomer is substituted with a nonpolar substituent. Since the antimicrobial activity arises from the amphiphilic character conferred by a periodic pattern of side chains rather than the precise spatial arrangement of side chains, other substitution patterns are also expected to produce facially amphiphilic polymers and they all are encompassed by the present invention. (see FIG. 7)

Polyamide and polyester homopolymers and copolymers of the present invention (FIG. 1) can be comprised solely of aromatic or heteroaromatic monomers or may include both aromatic and aliphatic monomers. One embodiment of the invention is a copolymer with aromatic monomers and α-amino acid monomers. The polyamides and polyesters can be constructed either by repetitively linking amino (or hydroxy) acid monomers (FIG. 1, I) or by alternating diamine (or dihydroxy) and dicarboxylic acid monomers (FIG. 1, II). While the majority of aromatic rings in the

examples depicted in FIGS. **1** and **2** have a meta substitution pattern, one skilled in the art would immediately appreciate that equivalent polymers could be designed with an ortho or a para orientation and these modifications can alter the conformation and the physical properties of the resulting polymer. Furthermore although the copolymers in FIG. **1** Ia and IIa–IIc are depicted with one polar and one nonpolar substituent, other substitution patterns are equally plausible. The optimal substitution patterns are determined by the conformational properties of the polymer backbone.

While polyamides and polyesters are the most common occurring examples of the present invention, other functional groups can be incorporated into the polymer backbone with similar results. In particular, thioamides and thioesters are anticipated to have very similar properties. The distance between aromatic rings can significantly impact the geometrical pattern of the polymer and this distance can be altered by incorporating aliphatic chains of varying length (FIG. **1**, IIc). Although IIc is depicted as a unsubstantiated alkylene chain, the alkylene chain can be optionally substituted or can comprise an amino acid, a dicarboxylic acid or a diamine. The distance between and the relative orientation of monomers also can altered by replacing the amide bond with a surrogate with additional atoms (FIG. **2**, XV–XVII). Thus replacing the carbonyl group with a dicarbonyl alters the distance between the monomers and the propensity of dicarbonyl unit to adopt an anti arrangement of the two carbonyl moiety and alter the periodicity of the polymer. Pyromellitic anhydride (FIG. **2**, IVg) represents still another alternative to simple amide linkages which can significant alter the conformation and physical properties of the copolymer (FIG. **1**, IVb).

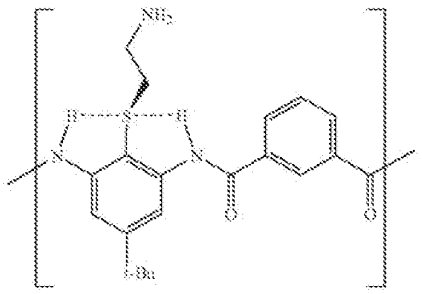
The synthetic processes can be modified to produce different ranges in molecular weight and the anti-microbial polymer of the present invention will have a molecular weight selected to impart physical and chemical properties optimized for the particular application being contemplated. Traditional polymer syntheses produce a product with a range of molecular weights. The polymer chemist will readily appreciate that the chain length of these polymers can be varied by techniques know in the polymer art. Polymers of the present invention can range in molecular weight from about 800 Daltons up to about 350 kiloDaltons. Advancements in solid-phase and solution phase synthesis of amino acid oligomers have made available techniques to prepare homogeneous polymers or oligomers with defined sequence and size and these techniques can be adapted to the present invention.

Polyureas (FIG. **3**, IVa), polycarbonates (FIG. **3**, IVb) or polyurethanes (FIG. **3**, IVc) are carbonic acid derivatives and exhibit properties similar to polyamides (N. Samson et al. *J. Appl. Polym. Sci.* 65, 2265 (1997)). FIG. **3** IVd and IVe depict two different substitution patterns which can be utilized. Other substitution patterns are equally effective.

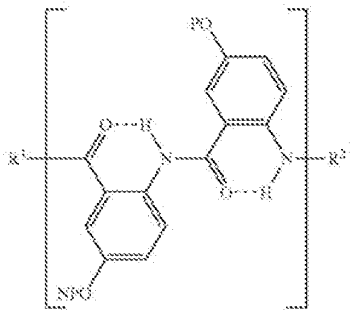
The polymer design process simply requires a structure in which the repeating sequence of monomers matches the secondary structure adopted by the backbone. Once the periodicity is observed, monomers substituted with polar and nonpolar groups monomers must be prepared and introduced to produce a cationic, amphiphilic secondary. Aromatic polyamides and ureas frequently have only a few torsional degrees of freedom per repeat (typically two or four). In this case the secondary structure adopted by these polymers is most likely planar with polar and nonpolar groups extended from opposite sides of the backbone. In some cases, the desired facial amphiphilicity can be achieved through a simple design principal.

Additional molecular features can be added to the macromolecular backbone to promote the desired secondary structure and disfavor other structures thereby combining elements of both positive and negative design. Conformational studies on biofoldamers (proteins and RNA), and early work with a variety of sequence-specific polymers, have shown that several elements are crucial in order for the polymers to adopt the desired folded conformation. Key elements include strong electrostatic interactions (i.e., intramolecular hydrogen bonding) between adjacent or more distant monomers and rigidification caused by the backbone torsions or by bulky functional groups. For example, the presence of multiple hydrogen bond donors and acceptors along the macromolecular backbone can lead to extensive intermolecular backbone interactions. Precise placement of well designed intramolecular interactions can stabilize desired secondary structures while at the same time blocking the backbone hydrogen bond donors which limits intermolecular aggregation problems. For example, in the polyurea and polyamide a thioether (FIG. **3**, XIa–c) was positioned between the two aromatic nitrogens to form an internal hydrogen bond between the sulfur and urea function. This limits the torsional angle of the aromatic carbon-urea NH bond by forcing the NH group to be on the same side as the heteroatom, thereby helping to define the overall sheet-like secondary structure. The secondary structure for this backbone is predicted to be nearly planar. Similarly, the poly-anthranilate polymer (XIII) is designed based on the finding of Hamuro and Hamilton (Y. Hamuro et al., J. Am. Chem. Soc. 1996 119:10587–93) that intramolecular hydrogen-bonding defines the secondary structure of this class of poly-arylamides.

(XIa-c)



(XIII)



Magainin and the other naturally occurring antibacterial peptides exhibit considerable variation in their chain length, hydrophobicity and distribution of charges. These linear peptides do, however, contain positively charges amino acids and a large hydrophobic moment resulting in a high propensity to adopt α-helical conformations in a hydrophobic environment, e.g., a cell surface or a natural or synthetic membrane. (Z. Oren and Y. Shai Biopolymers (Peptide Science). 1998 47, 451–463.) The periodic distribution of hydrophobic and hydrophilic side chains in their amino acid

sequences allows the segregation of the hydrophobic and hydrophilic side chains to opposite faces of the cylinder formed by the helix. The overall amphiphilicity, not the specific sequence, secondary structure or chirality, correlates best with anti-microbial activity. Thus it appears that any suitably amphiphilic material (not necessarily an α-helix or β-sheet) would have anti-microbial properties. The necessary condition for forming a facially amphiphilic structure is the molecule should have a repeating pattern of polar and nonpolar side chains whose periodicity is approximately the same as that of the secondary structure of interest.

The term "microorganism" as used herein includes bacteria, algae, fungi, yeast, mycoplasmids, parasites and protozoa.

The term "antimicrobial", "microbiocidal" or "biocidal" as used herein means that the materials inhibit, prevent, or destroy the growth or proliferation of microorganisms. This activity can be either bacteriocidal or bacteriostatic. The term "bacteriocidal" as used herein means the killing of microorganisms. The term "bacteriostatic" as used herein means inhibiting the growth of microorganisms which can be reversible under certain conditions.

The term "polymer" as used herein refers to a macromolecule comprising a plurality of repeating units or monomers. The term includes homopolymers, which are formed from a single type of monomers and copolymers that are formed from two or more different monomers. In copolymers the monomers may be distributed randomly (random copolymer), in alternating fashion (alternating copolymer) or in blocks (block copolymer). The polymers of the present invention are either homopolymers or alternating copolymers. The term "polymer" as used herein is intended to exclude proteins, peptides, polypeptides and other proteinaceous materials composed exclusively of α or β-amino acids. The term "oligomer" as used herein refers to a homogeneous polymer with a defined sequence and molecular weight.

The term "polymer backbone" or "backbone" as used herein refers to that portion of the polymer which is a continuous chain comprising the bonds formed between monomers upon polymerization. The composition of the polymer backbone can be described in terms of the identity of the monomers from which it is formed without regard to the composition of branches, or side chains, off the polymer backbone.

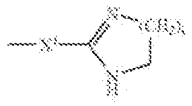
The term "polymer side chain" or "side chain" refers to portions of the monomer which, following polymerization, forms an extension off the polymer backbone. In homopolymers all the polymer side chains are derived from the same monomer. A copolymer can comprise two or more distinct side chains from different monomers.

The term "alkyl" as used herein denotes a univalent saturated branched or straight hydrocarbon chain. Unless otherwise stated such chains contain from 1 to 18 carbon atoms. Representative of such alkyl groups are methyl, ethyl, propyl, iso-propyl, sec-butyl, tert-butyl, pentyl, neopentyl, iso-pentyl, hexyl, iso-hexyl, heptyl, octyl, nonyl, decyl, tridecyl, tetradecyl, hexadecyl octadecyl, and the like. When qualified by "lower" the alkyl group will contain from 1 to 6 carbon atoms. The term "cycloalkyl" as used herein denotes a univalent cyclic hydrocarbon chain. Representative groups are cyclopropyl, cyclobutyl, cyclohexyl, cyclopentyl and cyclohexyl.

The phrase "groups with chemically nonequivalent termini" refers to functional groups such as esters amides, sulfonamides and N-hydroxyoximes where reversing the orientation of the substituents, e.g. $R^1C(=O)OR^2$ vs. $R^1O(O=)CR^2$, produces unique chemical entities.

The term "basic heterocycle" as used herein denotes cyclic atomic array which includes a nitrogen atom that has a pKa greater than about 5 and that is protonated under physiological conditions. Representative of such basic heterocycles are pyridine, quinoline, imidazole, imidazoline, cyclic guanidines, pyrazole, pyrazoline, dihydropyrazo line, pyrrolidine, piperidine, piperazine, 4-alkylpiperazine, and derivatives thereof such as 2-aminopyridine, 4-aminopyridine, 2-aminoimidazoline, 4-aminoimidazoline or VII where X^3 is O, N, S or absent and i is 2 to 4.

(VII)



The term "amphiphilic" as used herein describes a three-dimensional structure having discrete hydrophobic and hydrophilic regions. An amphiphilic polymer requires the presence of both hydrophobic and hydrophilic elements along the polymer backbone. The presence of hydrophobic and hydrophilic groups is a necessary, but not sufficient, condition to produce an amphiphilic molecule or polymer. Polymers frequently adopt a random or disordered conformation in which the side chains are located randomly in space and there are no distinctive hydrophobic and hydrophilic regions.

The term "facially amphiphilic" or "facial amphiphilicity" as used herein describes polymers with polar (hydrophilic) and nonpolar (hydrophobic) side chains that adopt conformation(s) leading to segregation of polar and nonpolar side chains to opposite faces or separate regions of the structure. This structure can comprise any of the energetically accessible low-energy conformations for a given polymer backbone. Additionally random or block copolymers may adopt random backbone conformations that do not lead to distinct hydrophilic and hydrophobic regions or which do not segregate along different faces of the polymer. These copolymers are not facially amphiphilic as defined herein.

The term "naturally occurring amino acids" means the L-isomers of the naturally occurring amino acids. The naturally occurring amino acids are glycine, alanine, valine, leucine, isoleucine, serine, methionine, threonine, phenylalanine, tyrosine, tryptophan, cysteine, proline, histidine, aspartic acid, asparagine, glutamic acid, glutamine, carboxyglutamic acid, arginine, ornithine and lysine. Unless specifically indicated, all amino acids referred to in this application are in the L-form.

The term "side chain of a naturally occurring amino acid" as used herein refers to the substituent on the a-carbon of a amino acid. The term "polar side chain of a naturally occurring amino acid" refers to the side chain of a positively charged, negatively charged or hydrophilic amino acid. The term "nonpolar side chain of a naturally occurring amino acid" refers to the side chain of a hydrophobic amino acid.

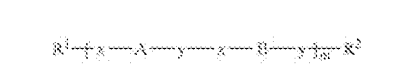
The term "positively charged amino acid" or "cationic amino acid" as used herein includes any naturally occurring or unnatural amino acid having a positively charged side chain under normal physiological conditions. Examples of positively charged naturally occurring amino acids are arginine, lysine and histidine.

The term "hydrophilic amino acid" means any amino acid having an uncharged, polar side chain that is relatively

soluble in water. Examples of naturally occurring hydrophilic amino acids are serine, threonine, tyrosine, asparagine, glutamine, and cysteine.

The term "hydrophobic amino acid" means any amino acid having an uncharged, nonpolar side chain that is relatively insoluble in water. Examples of naturally occurring hydrophobic amino acids are alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine.

One embodiment of the present invention is a polymeric compound of formula I



(I)

wherein:

x is NR^5, O, or S, y is C═O, C═S, O═S═O, or —C(═O)C(═O)— and R^5 is hydrogen, methyl or ethyl;

either both A and B are independently optionally substituted o-, m-, p-phenylene,

or optionally substituted heteroarylene wherein (i) A and B are both substituted with a polar (P) group and a nonpolar (NP) group, (ii) one of A and B is substituted with a polar (P) group and a nonpolar (NP) group and the other of A and B is substituted with neither a polar nor a nonpolar group, or (iii) one of A or B is substituted with a polar (P) group and the other of A or B is substituted with a nonpolar (NP) group; or,

one of A and B is o-, m-, p-phenylene or heteroarylene—the other of A and B is a C_3 to C_8 cycloalkyl or $(CH_2)_q$ where q is 1 to 7 wherein (i) one of A or B is optionally substituted by one or more polar (P) group(s) and the other of A or B is optionally substituted with one or more nonpolar (NP) group(s), or (ii) A is substituted with a polar (P) group and a nonpolar (NP) group and B is a C_3 to C_8 cycloalkyl or $(CH_2)_q$ where q is 1 to 7 and B is optionally independently substituted with one or more polar (P) or nonpolar (NP) group;

R^1 is (i) -y-C and R^2 is OH or NH_2 wherein C is selected from a group consisting of C_1–C_8 alkyl, vinyl, 2-propenyl, H-x-$(CH_2)_p$—, (C_1–C_8-alkoxy)C(═O)$(CH_2)_p$—, C_1–C_8 alkoxy, benzyloxy, t-butoxy, pyridine and phenyl said pyridine or phenyl optionally substituted with 1 or 2 substituents independently selected from a group consisting of halo, nitro, cyano, C_1–C_8 alkoxy, C_1–C_8 alkoxycarbonyl, and benzyloxycarbonyl; or, (ii) is H and R^2 is -x-$(CH_2)_p$—W wherein x is as defined above and p is as defined below and W is N-maleimide or V as defined below, or (iii) R_1 and R_2 together are a single bond;

NP is a nonpolar group an independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of hydrogen, C_1–C_{10} alkyl, C_3–C_{10} branched alkyl, C_3–C_8 cycloalkyl, monocyclic or polycyclic phenyl optionally substituted with one or more C_1–C_8 alkyl, C_1–C_8 alkoxy or halo groups and monocyclic or polycyclic heteroaryl optionally substituted with one or more C_1–C_8 alkyl, C_1–C_8 alkoxy, or halo groups and U and p are as defined below;

P is a polar group selected from a group consisting of IIa, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene

(IIa)

wherein,

U is absent or selected from a group consisting of O, S, S(═O), $S(═O)_2$, NH, —C(═O)O—, —C(═O)NH—, —C(═O)S—, —C(═S)NH—, —$S(═O)_2$NH—, and C(═NO—) wherein groups with two chemically nonequivalent termini can adopt both possible orientations;

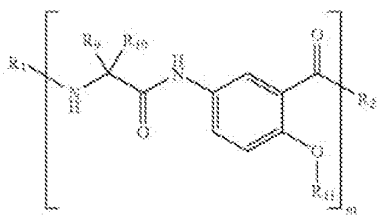
V is selected from a group consisting of amino, hydroxyl, thio, C_1–C_8 alkylamino, C_1–C_8 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, C_1–C_8 alkoxycarbonyl, basic heterocycle, and phenyl optionally substituted with an amino, C_1–C_8 alkylamino, C_1–C_8 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino;

and the alkylene chain is optionally substituted with an amino or hydroxyl group or unsaturated;

p is independently 0 to 8;

m is 2 to at least about 500.

Another embodiment of polymer compound of formula VII:



(VII)

wherein

one of R^9 or R^{10} and R^{11} is a polar (P) group and the other of R^9 or R^{10} and R^{11} is a nonpolar (NP) group;

P is a polar group selected from a group consisting of IIb, hydroxyethoxymethyl, methoxyethoxymethyl or polyoxyethylene

(IIb)

wherein:

V is selected from a group consisting of amino, hydroxyl, C_1–C_8 alicylamino, C_1–C_8 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_8 alkylamino, C_1–C_8 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino; and,

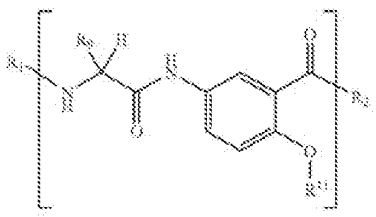
the alkylene chain is optionally substituted with an amino or hydroxyl group;

p is independently 0 to 8; and,

m is 2 to at least about 30.

Still another embodiment of the present invention is a polymeric compound of formula IX

(IX)



wherein:

one of R^9 or R^{11} is either a polar (P) group or a nonpolar (NP) group and the other of R^9 or R^{11} is the other of a polar (P) group or a nonpolar (NP) group;

NP is —$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of hydrogen, C_1–C_4 alkyl, C_3–C_{12} branched alkyl, C_3–C_8 cycloalkyl, phenyl optionally substituted with one or more C_1–C_4 alkyl groups C_1–C_4 alkoxy or halo groups and heteroaryl optionally substituted with one or more C_1–C_4 alkyl group, C_1–C_4 alkoxy or halo groups and p is as defined below;

P is a polar group selected from a group consisting of IIIb, hydroxyethoxymethyl, methoxyethoxymethyl or polyoxyethylene

—$(CH_2)_p$—V (IIIb)

wherein:

V is selected from a group consisting of amino, hydroxyl, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino; and,

the alkylene chain is optionally substituted with an amino or hydroxyl group.

p is independently 0 to 8.

An embodiment of the present invention is a polymeric compound of formula IX wherein R^9 is a polar side chain of a natural amino acids and R^{11} is selected from a group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, sec-pentyl, and benzyl.

Another embodiment of the present invention is polymeric compound of formula IX wherein R^9 is a nonpolar side chain of a natural amino acids and R^{11} is a polar group selected from a group consisting of IIIb, hydroxyethoxymethyl, methoxyethoxymethyl or polyoxyethylene

—$(CH_2)_p$—V (IIIb)

wherein:

V is selected from a group consisting of amino, hydroxyl, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino; and,

p is independently 0 to 8.

Still another embodiment of the present invention is a polymeric compound of formula I wherein:

x is NH and y is C═O or C═S;

A and B are independently optionally substituted o-, m-, or p-phenylene, 2,5-thiophenylene or 2,5-pyrrolene;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of hydrogen, C_1–C_4 alkyl, C_3–C_{12} branched alkyl, C_3–C_8 cycloalkyl, phenyl optionally substituted with one or more C_1–C_4 alkyl groups C_1–C_4 alkoxy or halo groups and heteroaryl optionally substituted with one or more C_1–C_4 alkyl group, C_1–C_4 alkoxy or halo groups and U and p are as defined below;

P is a polar group selected from a group consisting of IIIa, hydroxyethoxymethyl, methoxyethoxymethyl or polyoxyethylene

—U—$(CH_2)_p$—V (IIIa)

wherein:

U is absent, O, S, SO, SO_2, or NH;

V is selected from a group consisting of amino, hydroxyl, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino; and,

the alkylene chain is optionally substituted with an amino or hydroxyl group;

p is independently 0 to 8; and,

m is 2 to at least about 500.

An embodiment of the present invention is a polymeric compound of formula I wherein:

x is NR^3, R^3 is hydrogen, and y is C═O or C═S;

A and B are independently optionally substituted o-, m-, or p-phenylene;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of hydrogen, methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is absent or selected from a group consisting of O and S, and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, pyridine, piperidine, piperazine, 4-alkylpiperazine; and

p is independently 0 to 8;

m is 2 to at least about 500.

Another embodiment of the present invention is a polymeric compound of formula I wherein:

x is NR^3, y is CO, and R^3 is hydrogen;

A and B are m- or p-phenylene wherein (i) A is substituted at the 2-position with a polar (P) group and B is substituted at the 5-position with a nonpolar (NP) group, (ii) A is substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group and B is substituted at the 2-position with a nonpolar (NP) group and at the 5-position with a polar (P) group or, (iii) A is substituted at the 2-position with one of a polar (P) or nonpolar (NP) group and B is substituted at the 2-position with the other of a nonpolar (NP) or a polar (P) group;

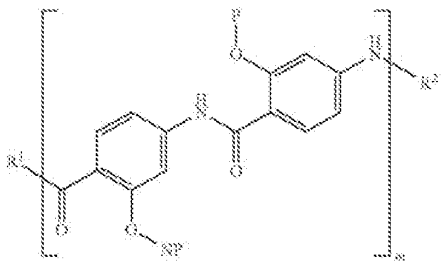
NP is a nonpolar group independently selected from R^4 or —U—R^4 wherein R^4 is selected from a group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

p is independently 0 to 8; and,

m is 2 to at least about 500.

Still another embodiment of the present invention is a polymeric compound of formula XII

(XII)



wherein:

NP is a nonpolar group independently selected from a group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

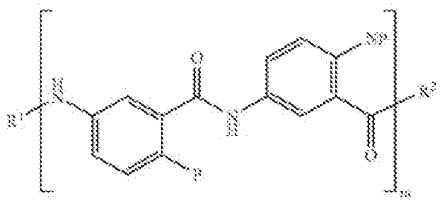
P is a polar group U—$(CH_2)_p$—V wherein U is selected from a group consisting of O, S, or no atom and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, and $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, 4-alkylpiperazine; and,

p is independently 0 to 8;

m is 2 to at least about 30.

Yet another embodiment of the present invention is a polymer according to claim 8 comprising a compound of formula XIV;

(XIV)



wherein:

NP is a nonpolar group independently selected from R^4 or —U—R^4 wherein R^4 is selected from a group consisting of methyl, ethyl, n-propyl, iso-propyl, 12-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is selected from a group consisting of O, S, or no atom and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, and $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, 4-alkylpiperazine; and,

p is independently 0 to 8;

m is 2 to at least about 30.

Yet another embodiment of the present invention is a polymeric compound of formula I wherein:

x is NR^3, y is CO, and R^3 is hydrogen;

A and B are o-phenylene wherein A is substituted at the 5-position with a polar (P) group and B is substituted at the 5-position with a nonpolar (NP) group;

NP is a nonpolar group independently selected from R^4 or —U—R^4 wherein R^4 is selected from a group consisting of methyl, ethyl, n-propyl, iso-propyl, iso-butyl, n-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

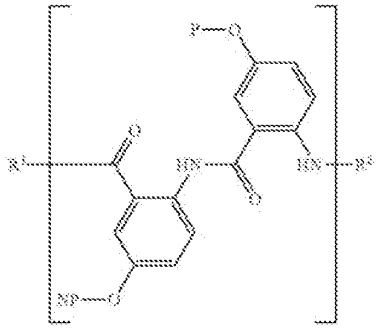
P is a polar group U—$(CH_2)_p$—V wherein U is selected from a group consisting of O, S, or no atom and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, and $N(CH_2CH_2NH_2)_2$, pyridine, piperidine, piperazine, 4-alkylpiperazine;

p is independently 0 to 8; and,

m is 2 to at least about 500.

Another embodiment of the present invention is a polymeric compound of formula XIII:

(XIII)



wherein:

NP is a nonpolar group independently selected from a the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

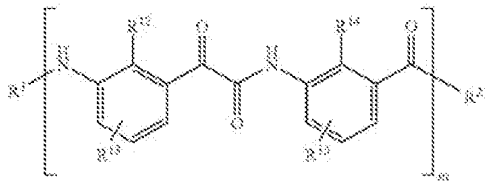
P is a polar group $(CH_2)_p$—V wherein V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, guanidine, piperazine, 4-alkylpiperazine;

p is independently 0 to 8;

m is 2 to at least about 30.

An embodiment of the present invention is a polymeric compound of formula XV:

(XV)



wherein

either R^{13} and R^{14} are independently polar (P) groups and R^{15} and R^{15} are independently nonpolar (NP) groups substituted at one of the remaining unsubstituted carbon atoms, or R^{13} and R^{14} are independently nonpolar (NP) groups and R^{15} and R^{15} are independently polar (P) groups

NP is a nonpolar group independently selected from R^4 or —U—R^4 wherein R^4 is selected from a the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and U is defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is selected from a group consisting of O or S and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, guanidine, pyridine, piperazine, 4-alkylpiperazine;

p is independently 0 to 8;

m is 2 to at least about 30.

An embodiment of the present invention is a polymeric compound of formula II wherein:

x and y can be (i) taken independently wherein x is NR^7, O, S, $(CR^7R^8)NR^9$, (CR^7R^8), or $(CR^7R^8)S$, y is C═O, C═S, C═S═O, —C(═O)C(═O)—, $(CR^7R^8)C$═O or $(CR^7R^8)C$═S, and R^7 is hydrogen, methyl or ethyl; or, (ii) taken together to be pyromellitic diimide; and R^7 and R^8 together are $(CH_2)_2NR^{12}(CH_2)_2$ and R^{12} is selected from a group consisting of hydrogen —C(═N)CH_3 or C(═NH)—NH_2; and R^7 and R^8 together are $(CH_2)_p$ wherein p is as defined below;

both A and B are independently optionally substituted o-, m-, p-phenylene, or optionally substituted heteroarylene wherein (i) A and B are both substituted with a polar (P) group and a nonpolar (NP) group, (ii) one of A and B is substituted with a polar (P) group and a nonpolar (NP) group and the other of A and B is substituted with neither a polar nor a nonpolar group, or (iii) one of A or B is substituted with a polar (P) group and the other of A or B is substituted with a nonpolar (NP) group;

R^1 is (i) —B-y-R^2 and R^2 is -x-$(CH_2)_p$—W wherein x is as defined above and W is hydrogen, phenyl optionally substituted with up to three substituents selected from a group consisting of halogen, C_1–C_4 alkyl, C_1–C_4 alkoxy, and carboxyl, N-maleimide, or V as defined below, and p is as defined below; or, (ii) R^1 and R^2 together are a single bond

NP is a nonpolar group an independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of hydrogen, C_1–C_{10} alkyl, C_3–C_{10} branched alkyl, C_3–C_8 cycloalkyl, monocyclic or polycyclic phenyl optionally substituted with one or more C_1–C_4 alkyl, C_1–C_4 alkoxy or halo groups and monocyclic or polycyclic heteroaryl optionally substituted with one or more C_1–C_4 alkyl, C_1–C_4 alkoxy, or halo groups and U and p are as defined below;

P is a polar group selected from a group consisting of IIIa, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene

—U—$(CH_2)_p$—V (IIIa)

wherein,

U is absent or selected from a group consisting of O, S, S(═O), S(═O)$_2$, NH, —C(═O)O—, —C(═O)NH—, —C(═O)S—, —C(═S)NH—, —S(═O)$_2$NH—, and C(═NO—) wherein groups with two chemically nonequivalent termini can adopt both possible orientations;

V is selected from a group consisting of amino, hydroxyl, thio, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_2NH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, C_1–C_6 alkoxycarbonyl, basic heterocycle, and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino;

and the alkylene chain is optionally substituted with an amino or hydroxyl group or unsaturated;

p is independently 0 to 8;

m is 2 to at least about 500.

Another embodiment of the present invention is a polymeric compound of formula II wherein:

x═NH and y═CO;

A and B are m- or p-phenylene wherein (i) A is substituted at the 2-position with a polar (P) group and B is substituted at the 5-position with a nonpolar (NP) group, or (ii) A is substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group and B is either substituted at the 2-position with a nonpolar (NP) group and at the 5-position with a polar (P) group or B is unsubstituted;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of methyl, ethyl, n-propyl, iso-propyl, iso-butyl, sec-butyl, tert-butyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is absent or selected from a group consisting of O and S, and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_2NH_2$, $N(CH_2CH_2NH_2)_2$, piperidine, 4-alkylpiperazine and,

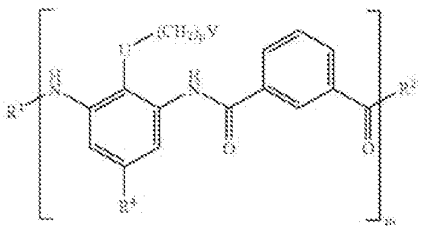
p is independently 0 to 8;

m is 2 to at least about 500.

Yet another embodiment of the present invention is a polymeric compound of formula II where A is an optionally substituted 1,3-diaminobenzene and B is an optionally substituted iso-phthalic acid.

Still another embodiment of the present invention is a polymeric compound of formula XI

(XI)



wherein:

R^3 is selected from a group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, ii-pentyl, iso-pentyl, and sec-pentyl;

U is O or S;

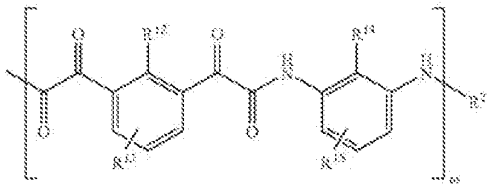
V is amino, lower alkyl amino, lower dialkylamino, guanidine;

p is independently 0-8;

m is 2 to at least about 30.

Another embodiment of the present invention is a polymeric compound of formula XVI

(XVI)



wherein:

either R^{12} and R^{14} are independently polar (P) groups and R^{13} and R^{15} are independently nonpolar (NP) groups substituted at one of the remaining unsubstituted carbon atoms, or R^{12} and R^{14} are independently nonpolar (NP) groups and R^{13} and R^{15} are independently polar (P) groups

NP is a nonpolar group independently selected from R^4 or —U—R^4 where R^4 is selected from a group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U is as defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is absent or selected from a group consisting of O and S, and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, piperidine, and 4-alkylpiperazine;

U is O or S;

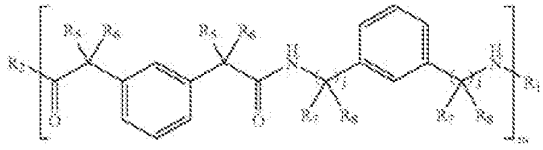
V is amino, lower alkyl amino, lower dialkylamino, guanidine;

p is independently 0 to 8; and

m is 2 to at least about 30.

Still another embodiment of the present invention is a polymeric compound of formula XX

(XX)



wherein j is independently 0 or 1, R^5 and R^6 together are $(CH_2)_2NH(CH_2)_2$ and R^7 and R^8 together are $(CH_2)_p$ wherein p is 4 to 6.

Yet another embodiment of the present invention is a polymeric compound of formula IV

(IV)

wherein:

x is NR^3 or NHNH and y is NR^3, NHNH, S or O, and R^3 is hydrogen, methyl or ethyl;

z is C═O, —(C═O)C(═O)—, C═S or O═S═O;

A and B are independently optionally substituted o-, m-, p-phenylene or optionally substituted heteroarylene wherein (i) A and B are both substituted with a polar (P) group and a nonpolar (NP) group (NP), (ii) one of A and B is substituted with a polar (P) group and a nonpolar (NP) group and the other of A and B is substituted with neither a polar nor a nonpolar group, or (iii) one of A or B is substituted with one or two polar (P) group(s) and the other of A or B is substituted with one or two nonpolar (NP) group(s), or, or (iv) A is substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group and B is unsubstituted;

R^1 is (i) —B-y-R^3 and R^2 is -x-$(CH_2)_p$—W wherein x is as defined above and W is hydrogen, pyridine and phenyl said pyridine or phenyl optionally substituted with 1 or 2 substituents independently selected from a group consisting of halo, nitro, cyano, C_1–C_6 alkoxy, C_1–C_6 alkoxycarbonyl, and benzyloxycarbonyl; R^1 is H and R^2 is -x-$(CH_2)_p$—V or (ii) R_1 and R_2 together are a single bond;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of C_1–C_{18} alkyl, C_3–C_{18} branched alkyl, C_3–C_8 cycloalkyl, monocyclic or polycyclic phenyl optionally substituted with one or more C_1–C_4 alkyl or halo groups, and monocyclic or polycyclic heteroaryl optionally substituted with one or more C_1–C_4 alkyl or halo groups and U and p are as defined below;

P is a polar group selected from a group consisting of IIIa, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene

—U—$(CH_2)_p$—V (IIIa)

wherein,

U is absent or selected from a group consisting of O, S, S(═O), $S(═O)_2$, NH, —C(═O)O—, —C(═O)NH—, —C(═O)S—, —C(═S)NH—, —$S(═O)_2$NH—, and C(═NO—) wherein groups with two chemically nonequivalent termini can adopt both possible orientations;

V is selected from a group consisting of amino, hydroxyl, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, basic heterocycle, and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino;

and the alkylene chain is optionally substituted with an amino or hydroxyl group or optionally unsaturated;

p is independently 0 to 8;

m is 2 to at least about 500.

Yet another embodiment of the present invention is a polymeric compound of formula IV wherein:

x and y are NR^3, z is C═O or C═S, and R^3 is hydrogen;

A and B are independently optionally substituted o-, m-, or p-phenylene;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of hydrogen, C_1–C_8 alkyl, C_3–C_{12} branched alkyl, C_3–C_8 cycloalkyl, phenyl optionally substituted with one or more C_1–C_8 alkyl groups and heteroaryl

optionally substituted with one or more C_1–C_4 alkyl groups and U and p are as defined below;

P is a polar group selected from consisting of IIIa, hydroxyethoxymethyl, methoxyethoxymethyl or polyoxyethylene

$$—U—(CH_2)_p—V \quad (IIIa)$$

wherein

U is O, S, S(=O), S(=O)$_2$, NH, or absent;

V is selected from a group consisting of amino, hydroxyl, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, and imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkcylamino;

and the alkylene chain is optionally substituted with an amino or hydroxyl group;

p is independently 0 to 8; and,

m is 2 to at least about 500.

An embodiment of the present invention is a polymeric compound of formula IV wherein:

x and y are NH, z is C=O;

A and B are m- or p-phenylene and either (i) A is substituted at the 2-position with a polar (P) group and B is substituted at the 5-position with a nonpolar (NP) group, or (ii) A is substituted at the 5-position with a polar (P) group and B is substituted at the 2-position with a nonpolar (NP) group, or (iii) A and B are both substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group, or (iv) A is substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group and B is unsubstituted;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of hydrogen, methyl, ethyl, n-propyl, iso-propyl, iso-butyl, sec-butyl, tert-butyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

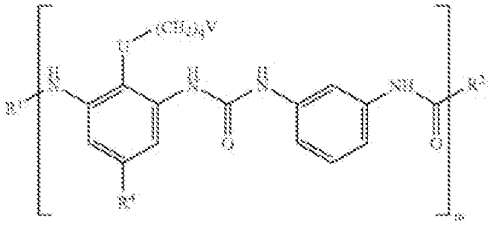
P is a polar group U—$(CH_2)_p$—V wherein U is absent or selected from a group consisting of O, S and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$ and $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, 4-alkylpiperazine;

p is independently 0 to 8; and,

m is 2 to at least about 500.

Another embodiment of the present invention is a polymeric compound of formula XIV

(XIV)



R^4 is selected from a group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

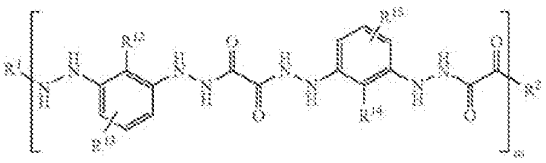
U is absent, O or S and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, and $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, 4-alkylpiperazine; and,

p is 0 to 8;

m is 2 to at least about 30.

Still another embodiment of the present invention is a polymeric compound of formula XVII

(XVII)



wherein:

either R^{12} and R^{14} are independently polar (P) groups and R^{13} and R^{15} are independently nonpolar (NP) groups substituted at one of the remaining unsubstituted carbon atoms, or R^{12} and R^{14} are independently nonpolar (NP) groups and R^{13} and R^{15} are independently polar (P) groups

NP is a nonpolar group independently selected from R^4 or —U—R^4 wherein R^4 is selected from a the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and U and p are as defined below;

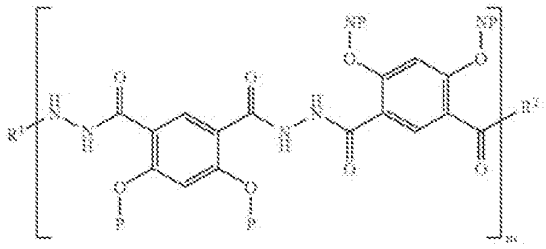
P is a polar group U—$(CH_2)_p$—V wherein U is selected from a group consisting of O or S and V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, guanidine, pyridine, piperazine, 4-alkylpiperazine;

p is independently 0 to 8; and,

m is 2 to at least about 30.

Another embodiment of the present invention is a polymeric compound of formula XVIII

(XVIII)



wherein:

NP is a nonpolar group independently selected from R^4 or —$(CH_2)_p$—R^4 wherein R^4 is selected from a group consisting of hydrogen methyl, ethyl, n-propyl, iso-

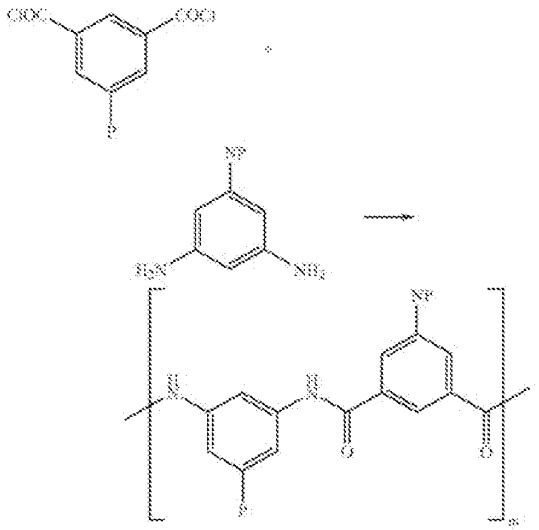
propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl and p is as defined below;

P is a polar group $(CH_2)_p$—V wherein V is selected from a group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, and $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, 4-alkylpiperazine,

p is independently 0 to 8; and,

m is 2 to at least about 30.

Polyamides and polyesters that are useful for the present invention can be prepared by typical condensation polymerization and addition polymerization processes. [G. Odian, *Principles of Polymerization*, John Wiley & Sons, Third Edition (1991), M. Steven, *Polymer Chemistry*, Oxford University Press, (1990)] Most commonly the polyamides are prepared by (a) thermal dehydration of amine salts of carboxylic acids, (b) reaction of acid chlorides with amines and (c) aminolysis of esters. Methods (a) and (c) are of limited use in polymerizations of aniline derivatives which are generally prepared utilizing acid chlorides. The skilled chemist, however, will recognize that there are many alternative active acylating agents, for example phosphoryl anhydrides, active esters or azides, which may replace an acid chloride and which, depending of the particular polymer being prepared, may be superior to an acid chloride. The acid chloride route is probably the most versatile and has been used extensively for the synthesis of aromatic polyamides



Homopolymers derived from substituted aminobenzoic acid derivatives (FIG. 1) can also prepared in a stepwise fashion. A stepwise process comprises coupling an N-protected amino acid to an amine (or hydroxy group) and subsequently removing the amine-protecting group and repeating the process. These techniques have been highly refined for synthesis of specific peptides, allow for the synthesis of specific sequences, and both solid-phase and solution techniques for peptide synthesis are directly applicable to the present invention. An alternative embodiment of the present invention is the corresponding polysulfonamides that can be prepared in analogous fashion by substituting sulfonyl chlorides for carboxylic acid chlorides.

The most common method for the preparation of polyureas is the reaction of diamines with diisocyanates. (Yamaguchi, I. et al. *Polym. Bull.* 2000 44, 247) This exothermic reaction can be carried out by solution techniques or by interfacial techniques. One skilled in organic and polymer chemistry will appreciate that the diisocyanate can be replaced with a variety of other bis-acylating agents e.g., phosgene or N, N'-(diimidazolyl)carbonyl, with similar results. Polyurethanes are prepared by comparable techniques using a diisocyanate and a dialcohol or by reaction of a diamine with a bis-chloroformate.

The syntheses of appropriately substituted monomers are straightforward. Numerous pathways are available to incorporate of polar and nonpolar side chains. Phenolic groups on the monomer can be alkylated. Alkylation of the commercially available phenol will be accomplished with standard Williamson ether synthesis for the non-polar side chain with ethyl bromide as the alkylating agent. Polar sidechains can be introduced with bifunctional alkylating agents such as $BOC\text{-}NH(CH_2)_2Br$. Alternatively the phenol group can be alkylated to install the desired polar side chain function by employing Mitsonobu reaction with $BOC\text{-}NH(CH_2)_2\text{—}OH$, triphenyl phosphine, and diethyl acetylenedicarboxylate. Standard conditions for reduction of the nitro groups and hydrolysis of the ester afford the amino acid. With the aniline and benzoic acid in hand coupling can be effected under a variety of conditions. Alternatively the hydroxy group of the (di)nitrophenol can be converted to a leaving group and functionality introduced under nucleophilic aromatic substitution conditions (FIG. 8). Other potential scaffolds that can be prepare with similar sequences are methyl 2-nitro-4-hydroxybenzoate (FIG. 9) and methyl 2-hydroxy-4-nitrobenzoate.

Antimicrobial testing is carried out using the micro-broth dilution technique with *E. coli*. Other organisms screened include ampicillin & streptomycin-resistant *E. coli* D31, *B. subtilis*, vancomycin-resistant *Enterococcus faecium* A436, and methicillin-resistant *S. aureus* 5332. Any peptide that is found to be active will be purified to homogeneity, and retested to obtain an accurate IC_{99}. Secondary screens include *Klebsiella pneumoniae* Kp1, and *Salmonella typhimunium* S5, and *Pseudomonas aeruginosa* 10. Traditionally, the micro-broth dilution technique only evaluates a single data point between 18–24 hours; however, the measurements can be extended to 24 hr to monitor cell growth through the entire growth phase. These experiments are performed in LB medium (which is a rich medium typically used to grow cells for protein expression) and represent a critical initial screen for activity. Since salt concentrations, proteins, and other solutes can affect the activities of antibiotics, materials that showed no activity in rich medium were retested in minimal medium (M9) to determine if rich medium was limiting activity. No relationship between the media and the activity was observed which is consistent with the mode of action is believed to be through general membrane disruption.

To determine the toxicity to mammalian, as well to bacterial, cells the biocidal activity is evaluated using both cultured cells and freshly obtained human blood cells. Increasing concentration of polymer will be added to both confluent and non-confluent cultures of human umbilical endothelial cells (HUVEC, Cambrex). Cell number, monolayer integrity, and cell viability (measured as trypan blue exclusion) will be evaluated as a function of time in culture.

While the synthesis of a variety of polymer backbones is well understood, computer-aided computational techniques can provide valuable insight and guidance in the selection of

potential antimicrobial polymers. The goal of these computations is to identify potential low energy conformations which have a geometrical repeat that matches a convenient sequence repeat of less than 6 monomer units. For example in α-amino acid oligomers, the geometrical repeat of the β-sheet is 2.0 residues. Once these repeating scaffolds are identified and the frequency of the repeat is calculated, polar and nonpolar substituents can be incorporated into the monomers to confer amphiphilic properties into the molecule.

High level ab initio calculations are one technique which will identify accessible low energy conformations. Unfortunately, these techniques, while extremely powerful, are not practical with molecules the size of the present invention. Molecular Dynamics simulations provide an alternative that can be adapted efficiently to molecules envisioned in the present invention. Key elements in determining conformational energies are strong electrostatic interactions (i.e., intramolecular hydrogen bonding) between adjacent or more distant monomers and rigidification caused by the backbone torsions or by bulky functional groups. In order to simulate these interactions in molecular mechanics calculations the empirical parameters, i.e., a force field, must be determined for representative polymer backbones. Density functional theory (DFT) can be used to carry out ab initio calculations on small model compounds that share the basic structural connectivity of the polymer backbones and which will generate required torsional potentials. The procedure to carry out these computations is:

1. Select simple model compounds that share similar torsional patterns with the target polymer backbones.
2. For each compound, perform a full geometric optimization at the BLYP/6–31G(d) level of theory (multiple initial configurations ensure the global minimum is obtained).
3. Calculate the single-point energy at the most stable geometry obtained in step 2 above, using B3LYP/6–311G++(dp) or plane wave CPMD.
4. Constrain a relevant torsion to a set angle and repeat steps 2 and 3.
5. Repeat step 4 for several angles; the torsional energy is obtained by subtracting the non-bonded interactions.
6. Fit energies versus torsion angle to a cosine series whose coefficients are the force field parameters.

After verifying the suitability of the force field by comparing computed predictions of the structure and thermodynamic properties to molecules that have similar torsional patterns and for which experimental data are available, the fitted torsions are then combined with bond stretching, bending, one-four, van der Waals, and electrostatic potentials borrowed from the CHARMM (B. R. Brooks et al. *J. Comp. Chem.* 1983 4:187–217 and TraPPE (M. G. Martin and J. I. Siepmann, *J. Phys. Chem B.* 1999 103:4508–17; C. D. Wick et al. *J. Phys. Chem B.* 2000 104:3093–3104) molecular dynamics force fields. To identify conformations that can adopt periodic folding patterns with polar groups and apolar groups lined up on the opposite sides. Initial structures can be obtained with the Gaussian package (M. Frisch et al. Gaussian 98 (revision A.7) Gaussian Inc., Pittsburgh, Pa. 1998). Then, the parallelized plane-wave Car-Parrinello CP-MD (R. Car and M. Parrinello *Phys. Rev. Lett.* 1985 55:2471–2474) program, (cf. U. Röthlisberger et al. *J. Chem. Phys.* 1996 3692–3700) is used to obtain energies at the minimum and constrained geometries. The conformations of the polymers without side-chains can be investigated in the gas phase. Both MD and MC methods will be used to sample the conformations. The former is useful for global motions of the polymer. With biasing techniques (J. I. Siepmann and D. Frenkel *Mol. Phys.* 1992 75:59–70; M. G. Martin and J. I. Siepmann *J. Phys. Chem. B* 1999 103:4508–4517; T. J. H. Vlugt et al. *Mol. Phys.* 1998 94:727–733) the latter allows efficient sampling for polymers with multiple local minimum configurations that are separated by relatively large barriers.

The potential conformations are examined for positions to attach pendant groups that will impart amphiphilic character to the secondary structure. Polymers selected from the gas-phase studies with suitable backbone conformations and with side-chains at the optimal positions to introduce amphiphilicity will be further evaluated in a model interfacial system, n-hexane/water, chosen because it is simple and cheap for calculations while it mimics well the lipid/water bilayer environment. Polymer secondary structures that require inter-polymer interactions can be identified by repeating the above-mentioned calculations using a periodically repeated series of unit cells of various symmetries (so called variable cell molecular dynamics or Monte Carlo technique) with or without solvent. The results of these calculations will guide the selection of candidates for synthesis.

An embodiment of the present is a computation technique to identify polymer backbones which can produce facially amphiphilic polymers by:

(1) selecting a polymer backbones or scaffolds suitable for regiospecific introduction of polar (P) and nonpolar (NP) groups;

(2) determining parameters for a molecular mechanics force field utilizing ab initio quantum mechanical calculations;

(3) calculating energetically accessible conformations of said backbone using molecular dynamics or molecular mechanics calculations;

(4) identifying energetically accessible conformations of said backbone wherein the periodicity of a geometrical/conformational repeat matches a sequence repeat;

(5) synthesizing monomers with polar and nonpolar substituents;

(6) synthesizing an antimicrobial polymer containing said monomers by solution or solid-phase synthesis.

The facially amphiphilic polymers of the present invention can have a substantial range in molecular weight. Facially amphiphilic molecules with molecular weights of about 0.8 kD to about 20 kD will be more prone to leach from the surface of the substrate. The facially amphiphilic polymer may be attached to, applied on or incorporated into almost any substrate including but not limited to woods, paper, synthetic polymers (plastics), natural and synthetic fibers, natural and synthetic rubbers, cloth, glasses and ceramics by appropriate methods including covalent bonding, ionic interaction, coulombic interaction, hydrogen bonding or cross-linking. Examples of synthetic polymers include elastically deformable polymers which may be thermosetting or thermoplastic including, but not limited to polypropylene, polyethylene, polyvinyl chloride, polyethylene terephthalate, polyurethane, polyesters, such as polylactide, polyglycolide, rubbers such as polyisoprene, polybutadiene or latex, polytetrafluoroethylene, polysulfone and polyethylenesulfone polymers or copolymers. Examples of natural fibers include cotton, wool and linen.

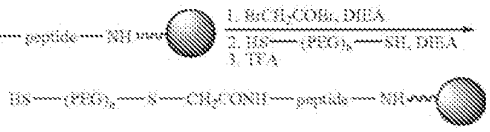
The polymers of the present invention thus provide a surface-mediated microbicide that only kills organisms in contact with the surface. Moreover the polymers of the present invention are stable and retain their bioactivity for extended periods of time. Polymers bound to the surface will

not leach out of the surface into the environment. Specificity can be imparted for microbial cell walls which can provide polymers with reduced toxicity to birds, fish, mammals and other higher organisms.

Any object that is exposed to or susceptible to bacterial or microbial contamination can be treated with these polymers. These needs are particularly acute in the health care and food industries. A growing concern with preservatives has produced a need for new materials that prevent microbiological contamination without including preservatives. The incidence of infection from food-borne pathogens is a continuing concern and antimicrobial packaging material, utensils and surfaces would be valuable. In the health care and medical device areas the utility of antimicrobial instruments, packaging and surfaces are obvious. Products used internally or externally in humans or animal health including, but not limited to, surgical gloves, implanted devices, sutures, catheters, dialysis membranes, water filters and implements, all can harbor and transmit pathogens. The polymers of the present invention can be incorporated into spinnable fibers for use in materials susceptible to bacterial contamination including fabrics, surgical gowns, and carpets. Ophthalmic solutions and contact lenses easily become contaminated and cause ocular infections. Antimicrobial storage containers for contact lens and cleaning solutions would be very valuable. Both pets and agronomic animals are exposed to and harbor a variety of infectious pathogenic organisms that can cause disease in animals or humans.

Traditionally, monolayers have been created at air/water interfaces and transferred to a variety of surfaces for chemical and structural characterization, as documented in a large body of work dating back to the seminal studies of Blodgett and Langmuir. Monolayers can be chemically bonded to solid supports, resulting in stable, uniformly packed molecular layers that self-assemble by absorption. Typically, these Self-Assembled Monolayers (SAMS) are covalently tethered to solids using either alkylsiloxane or thiolate-gold linkages (for reviews see M. Mrksich, *Cell Mol Life Sci.* 1998 54:653–62; M. Mrksich, and G. M. Whitesides *Ann Rev Biophys Biomol Struct.* 1996 25:55–78). Alkylthiolate-gold linkages can be formed on the surface of gold by spontaneous absorption of a thiol or disulfide. Gold layers can be deposited on most solid surfaces, providing great versatility. Alkylsiloxane monolayers can be prepared by reacting trialkoxysilanes or trichlorosilanes with a silicon dioxide surface resulting in a monolayer of crosslinked siloxanes on the surface. Siloxane monolayers may be formed on any solid that contains surface silanol groups including atomically smooth, surface-oxidized silicon wafers, glass and quartz. These two chemistries will allow amphiphilic polymers to be attached a variety of surfaces.

These amphiphilic polymers can incorporate linkers to allow the polymers to more efficiently interact with the environment around the solid surface. Tethering chemistries that allow presentation of peptides and proteins in native conformations with minimal interaction with the underlying substrate have been described. For examples, alkanethiols of the general form, $HS-(CH_2)_{11}-(OCH_2-CH_2)_n-OH$ (denoted $HS-C_{11}-E_n$, n=3–6), have now come into widespread use for studies of receptor/ligand interactions (M. Mrksich *Cell Mol. Life Sci.* 1998 54:653–62; M. Mrksich and G. M. Whitesides *Ann. Rev. Biophys. Biomol. Struct.* 1996 25:55–78). Polyethylene glycol derived amino acids, e.g. Fmoc-NH—$(CH_2-CH_2-O)_2CH_2$—COOH (Neosystems) have also been described Cys will be appended to the N-terminus to act as a group that allows coupling via its thiol, directly or through chemoselective ligation (T. W. Muir et al. *Methods Enzymol.* 1997 289:266–98; G. G. Kochendoerfer et al. *Biochemistry* 1999 38:11905–13). The thiol group serves to tether the molecule to gold surfaces, while the terminal hydroxyl and ethylene glycol groups project towards solvent, presenting a hydrophilic surface. Attachment to siloxane and polyethylene surfaces have also been described. (S. P. Massia and J. Stark *J. Biomed. Mat. res.* 2001 56:390–9; S. P. Massia and J. A. Hubbell *J. Cell Biol.* 1991 114:1089–1100; S. P. Massia and J. A. Hubbell *Anal. Biochem.* 1990 187:292–301; B. T. Houseman and M. Mrksich *Biomaterials* 2001 22:943–55).



Resin bound intermediates can easily be modified to incorporate linkers. Glass surfaces can be modified to allow reaction with the thiol groups of the peptide by: (i) aminoalkylation of the glass surface by treatment with trimethoxysilylpropylamine; (ii) reaction of the amino groups with a bromoacetyl bromide or other heterobifunctional crosslinker groups capable of also reacting with a thiol group. In the above example, we show an amino surface in which we have introduced bromoacetyl groups for subsequent reaction with peptide thiols. Alternatively, thiol-reactive maleimides, vinyl-sulfones (Michael acceptors) may be incorporated using commercially available cross-linking agents. Alternatively, the surface amino groups may be converted to carboxylates by treatment with an anhydride, and then converted to thioesters under standard conditions. The resulting thioesters react facilely and with extreme regioselectivity with an N-terminal Cys residue. By incorporating quantities of inactive "filler" molecule, e.g. one example which is not limiting is a monofunctional thiol-terminated short chain polyethylene glycol polymer with the reactive tethering group the molar ratio of the oligomer to the "filler" component, it should be possible to continuously vary the surface density of the polymers attached to a solid support.

An embodiment of the present invention is a process for producing an antimicrobial surface by attaching a antimicrobial facially amphiphilic polymer to a surface comprising treating said surface with a first chemically reactive group and reacting a facially amphiphilic polymer linked to a second reactive group thereto.

Another embodiment of the present invention is a process for attaching a facially amphiphilic polymer to a surface wherein the solid surface is treated with a 1-(trialkoxysilyl) alkylamine and facially amphiphilic polymer contains an activated carboxylic acid.

Yet another embodiment of the present invention is a process for attaching a facially amphiphilic polymer to a surface wherein the solid surface is treated with a ω-(trialkoxysilyl)alkyl bromoacetamide and facially amphiphilic polymer contains a thiol.

Another embodiment of the present invention is a process for attaching a facially amphiphilic polymer to a surface wherein the solid surface is treated with a N-[ω-(trialkoxysilyl)alkyl]maleimide and facially amphiphilic polymer contains a thiol.

Still another embodiment of the present invention is a process for attaching a facially amphiphilic polymer to a

surface wherein the surface is gold and the facially amphiphilic polymer contains a thiol.

A variety of polymers are used in a host of medical applications which require sterile surfaces. Catheters, like venous or urinary catheters are cause serious infections. Polyurethane based tubing is by far the major source of commercial catheter tubing. Amphiphilic polymers can be incorporated into polyurethane and other polymers using pre- and post manufacture techniques. The advantage of pre-manufacture incorporation is simpler modification strategies and dispersion of the antimicrobial agent throughout the tubing materials. Tubing manufacturing is typically an extrusion process in which pellets of polyurethane are heated and pressed through a dye producing tubing of the desired diameter. The thermal stability of urethane bonds is very similar to amide and urea bonds again suggesting that thermal processed conditions should not be a problem. For the pre-manufacture approach, designed antimicrobial polymers are added to the original polyurethane pellets before extrusion resulting in a uniform dispersion throughout the extruded polymer.

Post-manufacture modifications are also possible although in this case the antimicrobial polymer will only be present on the surface of the tubing. However, since catheters have a minimal life cycle it is likely that surface treatment will render the materials sufficiently sanitary for their application. There are a variety of methods one can use to modify polymeric surfaces (E. Piskin *J. Biomat. Sci.-Polymer Ed.* 1992 4:45–60). The most common technique to covalent attach a amphiphilic polymer to the surface relies on irradiation to produce free radicals that form covalent bonds between the polymer and active surface agent. Unfortunately, this process is completely random with no control over orientation or functional group attachment to the surface. Alternatively, photo or chemical oxidation of the polyurethane surface can create carboxylic acid or alcohol functionality which will be reactive toward these antimicrobial polymers (the cationic side chains or cationic end groups). The most common technique for surface oxidation is plasma etching (E. Piskin loc. cit.; S. H. Hsu and W. C. Chen, *Biomaterials* 2000 21:359–67) although ozone can also be used. After oxidation, the surface is treated with a bifunctional epoxide followed by addition of the cationic antimicrobial polymer which can react with the epoxide.

Microbial growth in paint and on the surface of paint films also remains an unsolved problem. This can occur in the wet formulated paint or by microbial growth on the dried surface. The paint industry currently uses either isothiazolones or "formaldehyde releasers" for wet paint protection from microbes (G. Sekaran et al. *J. Applied Polymer Sci.* 2001 81:1567–1571; T. J. Kelly et al. *Environ. Sci. Technol.* 1999 33:81–88; M. Sondossi et al. *International Biodeterioration & Biodegradation* 1993 32:243–61). Both of these products are harmful to human beings and great lengths and expense are taken at the factory to limit employee exposure; however, there is no viable alternative currently for the industry. Isothiazolones are used mainly for their effectiveness against *Pseudomonas aeruginosa* and that the antimicrobial polymers discussed in preliminary data are active against this strain.

Any object that is exposed to or susceptible to bacterial or microbial contamination can be treated with these polymers. These needs are particularly acute in the health care and food industries. A growing concern with preservatives has produced a need for new materials that prevent microbiological contamination without including preservatives. The incidence of infection from food-borne pathogens is a continuing concern and antimicrobial packaging material, utensils and surfaces would be valuable. In the health care and medical device areas the utility of antimicrobial instruments, packaging and surfaces are obvious. Products used internally or externally in humans or animal health including, but not limited to, surgical gloves, implanted devices, sutures, catheters, dialysis membranes, water filters and implements, all can harbor and transmit pathogens. The polymers of the present invention can be incorporated into spinnable fibers for use in materials susceptible to bacterial contamination including fabrics, surgical gowns, and carpets. Ophthalmic solutions and contact lenses easily become contaminated and cause ocular infections. Antimicrobial storage containers for contact lens and cleaning solutions would be very valuable. Both pets and agronomic animals are exposed to and harbor a variety of infectious pathogenic organisms that can cause disease in animals or humans.

An embodiment of the current invention is a antimicrobial composition comprising a facially amphiphilic polymer and a composition selected form the group consisting of paint, coatings, lacquer, varnish, caulk, grout, adhesives, resins, films, cosmetic, soap and detergent.

Another embodiment of the present invention is an improved catheter, the improvement comprising incorporating or attaching a facially amphiphilic polymer therein or thereto.

Yet another embodiment of the present invention is an improved contact lens, the improvement comprising incorporating or attaching an amphiphilic polymer therein or thereto.

An embodiment of the present invention is improved plastic devices for the hospital and laboratory the improvement comprising incorporating or attaching a facially amphiphilic polymer therein or thereto.

A further embodiment of the present invention is an improved woven and nonwoven fabrics for hospital use the improvement comprising the incorporating or attaching a facially amphiphilic polymer therein or thereto.

The following examples will serve to further typify the nature of this invention but should not be construed as a limitation in the scope thereof, which scope is defined solely by the appended claims.

EXAMPLE 1

Polyamide FIG. **6** XIa

2,6-Dinitro-4-t-butyl-phenyl (4-methyl)-benzenesulfonate (11)

2,6-dinitro-4-t-butyl-phenol (80 mmol; 10) and tosyl chloride (80 mmol) were dissolved in 300 ml CH_2Cl_2. Diisopropylethylamine (DIEA, 80 mmol) was added to the solution. The mixture was stirred at room temperature for 2 hours. The solution was washed with 10% citric acid, saturated aqueous NaCl (sat. NaCl), and dried with $MgSO_4$. The solvent was removed under reduced pressure, and the product was obtained as a bright yellow solid in quantitative yield. ^1H NMR (500 MHz, $CDCl_3$): δ=8.12 (s, 2H), 7.80 (d, 2H), 7.40 (d, 2H), 2.51(s, 3H), 1.41 (s, 9H). ESI-MS: m/z: 417.2 ($M+Na^+$).

2,6-Dinitro-4-t-butyl-1-(2-t-butoxycarbonylaminoethyl)-sulfanylbenzene (12).

Compound 11 (13 mmol), 2-Boc-aminoethanthiol (16 mmol) and DIEA(13 mmol) were dissolved in 50 ml chloroform. The solution was stirred under nitrogen for 12 hours. The solution was washed with 0.5 M NaOH, 10% citric acid,

sat. Na_2CO_3 and sat. NaCl, and dried with $MgSO_4$. The solution volume was reduced to 15 ml by rotary evaporation. After addition of 80 ml hexane the product crystallized as a bright yellow solid in. 94% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.81 (s, 2H), 4.87 (s, 1H), 3.31 (t, 2H), 3.10 (t, 2H), 1.44 (s, 9H), 1.39 (s, 9H). ESI-MS: m/z: 422.4 ($M+Na^+$).

2,6-Diamino-4-t-butyl-1-(2-t-butoxycarbonylaminoethyl) sulfanylbenzene (13)

Dinitro compound 12 (20 mmol) and sodium acetate (200 mmol) were added to 80 ml EtOH. The mixture was heated to 78° C., and the solid dissolved completely. Stannous chloride dihydrate (200 mmol) was added to the solution, and the reaction mixture was stirred at 78° C. for 35 minutes. After removal of solvent under reduced pressure, the residue was dissolved in 800 ml EtOAc, and washed with 40% KCO_3. The organic phase was dried, evaporated and the residue column chromatographed (SiO_2) and eluted with a gradient of CH_2Cl_2/MeOH from 100:1 to 95:5 to produce 13 in 93% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 6.21 (s, 2H), 5.41 (s, 1H), 4.35 (br, 4H), 3.21 (t, 2H), 2.75 (t, 2H), 1.35 (s, 9H), 1.24 (s, 9H). ESI-MS: m/z: 340.5 (MH^+).

General Method of Polymerization.

Diamine 13 (0.1 mmol) was dissolved in 3 ml DMF. Isophthaloyl dichloride (0.1 mmol), triethylamine (0.2 mmol)) and N,N-dimethylethylenediamine (0.2/n mmol) were added while stirring. The mixture was stirred under nitrogen for 18 hours. After the volume of solvent was reduced to 1 ml, water was added to precipitate the polymer. The polymer was collected and dried under vacuum. The Boc group was removed by treatment with trifluoroacetic acid (TFA, 3 ml) for 1 hour. The deprotected polymer was dried under vacuum overnight.

EXAMPLE 2

Solid Phase Synthesis of Oligomers XIb and XIc (FIG. 6)

Fmoc-PAL-PEG-resin (0.1 mmol) was swelled in DMF; then the Fmoc was removed with 20% piperidine in DMF for 20 min. The oligomer was then built up by alternately coupling 10 equivalents of isophthalic acid or diamine 10. In each case the couplings were carried out in DMF using 10 equivalents each of 2-(1H-benzotriazole-1-yl)-1,1,3,3,-tetramethyluronium hexafluorophosphate (HBTU) and N-hydroxybenzotriazole hydrate (HOBt), and 20 equivalents of DIEA for 24 hours at room temperature. The oligomers were cleaved from the resin by treatment with TFA/anisole (95:5) for 1 hour. Pure oligomers were obtained by HPLC on a reverse phase C4 column, with a linear gradient from 30% to 80% solvent B in 50 minutes (solvent A, 0.1% TFA in water; solvent B, acetonitrile/water/TFA 900:99:1). MALDI-TOF MS: XIb: 756.5 ($M+H^+$), XIc: 1125.6.($M+H^+$).

EXAMPLE 3

General Method for Amide Polymerization

An oven-dried flask is charged with diamine dissolved in dimethylsulfoxide (DMSO). To this solution is added an equimolar quantity of the diacid chloride which is freshly prepared by stirring the dicarboxylic acid with excess thionyl chloride for 2 hr prior to addition to the diamine solution. A catalytic amount of 4-dimethylaminopyridine and four-fold molar excess of triethylamine are added to the stirring mixture. The reaction is stirred at room temperature overnight under positive N_2 pressure. The DMSO solution is poured into water and the solid polymer is recovered by filtration. The degree of polymerization is controlled by the addition of various molar amounts of a monofunctional amine. The molar amount of the monofunctional amine is determined by the Flory equation (G. Odian, *Principles of Polymerization*, John Wiley & Sons, Third Edition (1991) p.78–82).

EXAMPLE 4

General Method for Urea Polymerization

A dried flask is charged with equal molar ratios of the diamine and the diisocyanate in DMSO. The reaction is stirred at room temperature overnight under positive N_2 pressure. The reaction is poured into water or ether and the solid polymer is recovered by filtration. The degree of polymerization is controlled by the addition of various molar amounts of a monofunctional amine. The molar amount of the monofunctional amine is determined by the Flory equation.

EXAMPLE 5

Antimicrobial Assays

The inhibition studies will be carried out in suspension using BHI medium inoculated with bacteria (10^6 CFU/ml) in a 96-well format. A stock solution of the polymers was prepared DMSO/water and used to prepare a ten fold dilution series. Minimal inhibitory concentrations (MIC) were obtained by incubating the compounds with the bacteria for 18 hours at 37° C., and measuring cell growth by monitoring at 590 nm. Antibacterial data is described in FIGS. 10 and 11.

EXAMPLE 6

Hemolytic Activity

The toxicity of the polymers to mammalian cells was evaluated with human blood, anticoagulated with 0.1 volume of sodium citrate, obtained from healthy volunteers. Washed erythrocytes are suspended in either HEPES buffer, pH 7.4, containing 1 mM Mg^{2+} and 1 mM Ca^{2+} or in heated and unheated autologous serum obtained from clotted blood. Red cell agglutination will be evaluated microscopically and red cell lysis will be evaluated by measuring the amount of released hemoglobin spectroscopically. The effect of polymers on platelet function will be studied by adding increasing concentrations of polymer to citrate-anticoagulated platelet-rich plasma. Platelet aggregation and secretion will then be studied in a lumi-aggregometer (Chrono-Log).

All references cited in the application are hereby incorporated in their entirety into this specification. Numerous modifications and alternative embodiments of the invention will be apparent to those skilled in the art in view of the foregoing description. Accordingly, this description is to be construed as illustrative only and is for the purpose of teaching those skilled in the art the best mode of carrying out the invention. Details of the structure may be varied substantially without departing from the spirit of the invention and the exclusive use of all modifications which come within the scope of the appended claim is reserved.

The invention claimed is:

1. A polymer or oligomer comprising a compound of formula I

(I)

wherein:

x is NR^3, O, or S; y is C═O, C═S, O═S═O, or —C(═O)C(═O)—; and R^3 is hydrogen, methyl or ethyl;

either both A and B are independently optionally substituted o-, m-, p-phenylene, or optionally substituted heteroarylene wherein (i) A and B are both substituted with a polar (P) group and a nonpolar (NP) group, (ii) one of A and B is substituted with a polar (P) group and a nonpolar (NP) group and the other of A and B is substituted with neither a polar nor a nonpolar group, or (iii) one of A or B is substituted with a polar (P) group and the other of A or B is substituted with a nonpolar (NP) group; or,

one of A and B is o-, m-, p-phenylene or heteroarylene and the other of A and B is a C_3 to C_8 cycloalkyl or $(CH_2)_q$ where q is 1 to 7 wherein (i) one of A or B is optionally substituted by one or more polar (P) group(s) and the other of A or B is optionally substituted with one or more nonpolar (NP) group(s), or (ii) A is substituted with a polar (P) group and a nonpolar (NP) group and B is a C_3 to C_8 cycloalkyl or $(CH_2)_q$ where q is 1 to 7 and B is optionally independently substituted with one or more polar (P) or nonpolar (NP) group;

R^1 is (i) -y-C and R^2 is OH or NH_2 wherein C is selected from the group consisting of C_1–C_6 alkyl, C_1–C_6 haloalkyl, vinyl, 2-propenyl, H-x-$(CH_2)_p$—, $(C_1$–C_6-alkoxy)C(═O)$(CH_2)_p$—, C_1–C_8 alkoxy, benzyloxy, t-butoxy, pyridine and phenyl said pyridine or phenyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, C_1–C_6 alkoxy, C_1–C_6 alkoxycarbonyl, and benzyloxycarbonyl; or, (ii) is H and R^2 is -x-$(CH_2)_p$—W wherein x is as defined above and p is as defined below and W is H, N-maleimide or V as defined below, or (iii) -y-C and R^2 is -x-$(CH_2)_p$—W, or (iv) R^1 and R^2 together are a single bond;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from the group consisting of hydrogen, C_1–C_{10} alkyl, C_1–C_8 haloalkyl, C_3–C_8 branched alkyl, C_3–C_8 cycloalkyl, and monocyclic or polycyclic phenyl optionally substituted with one or more C_1–C_4 alkyl, C_1–C_4 alkoxy or halo groups and monocyclic or polycyclic heteroaryl optionally substituted with one or more C_1–C_8 alkyl, C_1–C_3 alkoxy, or halo groups and U and p are as defined below;

P is a polar group selected from the group consisting of IIIa, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene,

(IIIa)

wherein:

U is absent or selected from the group consisting of O, S, S(═O), $S(═O)_2$, NH, —C(═O)O—, —C(═O)NH—, —C(═O)S—, —C(═S)NH—, —$S(═O)_2$NH—, and C(═NO—) wherein groups with two chemically nonequivalent termini can adopt both possible orientations;

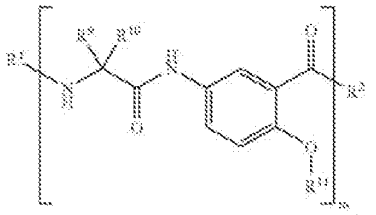
V is selected from the group consisting of amino, hydroxyl, thio, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, C_1–C_8 alkoxycarbonyl, basic heterocycle, and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino;

and the alkylene chain is optionally substituted with an amino or hydroxyl group or unsaturated;

p is independently 0 to 8; and

m is 2 to at least about 500.

2. The polymer or oligomer of claim 1, wherein said polymer or oligomer comprises a compound of formula VII

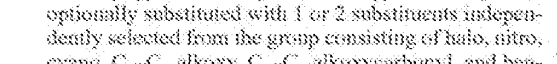


(VII)

wherein:

one of R^9 or R^{10} and R^{11} is a polar (P) group and the other of R^9 or R^{10} and R^{11} is a nonpolar (NP) group;

P is a polar group selected from the group consisting of IIIb, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene,



(IIIb)

wherein:

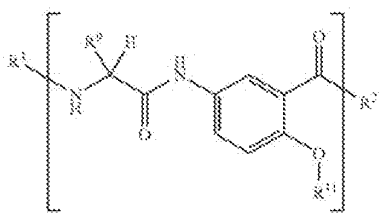
V is selected from the group consisting of amino, hydroxyl, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino; and,

the alkylene chain is optionally substituted with an amino or hydroxyl group;

p is independently 0 to 8; and

m is 2 to at least about 30.

3. The polymer or oligomer of claim 2, wherein said polymer or oligomer comprises a compound of formula IX



(IX)

wherein:

one of R^2 or R^{11} is either a polar (P) group or a nonpolar (NP) group and the other of R^2 or R^{11} is the other of a polar (P) group or a nonpolar (NP) group;

NP is $—(CH_2)_p—R^4$ wherein R^4 is selected from the group consisting of hydrogen, C_1–C_6 alkyl, C_3–C_{12} branched alkyl, C_3–C_8 cycloalkyl, and phenyl optionally substituted with one or more C_1–C_6 alkyl group, C_1–C_6 alkoxy or halo groups and heteroaryl optionally substituted with one or more C_1–C_4 alkyl group, C_1–C_4 alkoxy or halo groups and p is as defined below;

P is a polar group selected from the group consisting of IIIb, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene.

$$—(CH_2)_p—V \quad \text{(IIIb)}$$

wherein:

V is selected from the group consisting of amino, hydroxyl, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino;

the alkylene chain is optionally substituted with an amino or hydroxyl group; and

p is independently 0 to 8.

4. The polymer or oligomer of claim **3**, wherein R^5 is a polar side chain of a natural amino acid and R^{11} is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, sec-pentyl, and benzyl.

5. The polymer or oligomer of claim **3**, wherein R^5 is a nonpolar side chain of a natural amino acid and R^{11} is a polar group selected from the group consisting of IIIb, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene,

$$—(CH_2)_p—V \quad \text{(IIIb)}$$

wherein:

V is selected from the group consisting of amino, hydroxyl, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino; and

p is independently 0 to 8.

6. The polymer or oligomer of claim **1**, wherein:

x is NH and y is C═O or CS;

A and B are independently optionally substituted o-, m-, or p-phenylene, 2,5-thiophenylene or 2,5-pyrrolene;

NP is a nonpolar group independently selected from R^5 or $—U—(CH_2)_p—R^4$ wherein R^4 is selected from the group consisting of hydrogen, C_1–C_4 alkyl, C_3–C_{12} branched alkyl, C_3–C_8 cycloalkyl, phenyl optionally substituted with one or more C_1–C_4 alkyl groups, C_1–C_4 alkoxy or halo groups, and heteroaryl optionally substituted with one or more C_1–C_4 alkyl groups, C_1–C_4 alkoxy or halo groups, and U and p are as defined below;

P is a polar group selected from the group consisting of IIIa, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene,

$$—U—(CH_2)_p—V \quad \text{(IIIa)}$$

wherein:

U is absent, O, S, SO, SO_2, or NH;

V is selected from the group consisting of amino, hydroxyl, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino; and,

the alkylene chain is optionally substituted with an amino or hydroxyl group;

p is independently 0 to 8; and

m is 2 to at least about 500.

7. The polymer or oligomer of claim **1**, wherein:

x is NR^3, R^3 is hydrogen, and y is C═O or CS;

A and B are independently optionally substituted o-, m-, or p-phenylene;

NP a nonpolar group independently selected from R or $—U—(CH_2)_p—R^4$ wherein $R^4$is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

P is a polar group $U—(CH_2)_p—V$ wherein U is absent or selected from the group consisting of O and S, and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, pyridine, piperidine, piperazine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 500.

8. The polymer or oligomer of claim **7**, wherein:

x is NR^3, y is CO, and R^3 is hydrogen;

A and B are m- or p-phenylene wherein (i) A is substituted at the 2-position with a polar (P) group and B is substituted at the 5-position with a nonpolar (NP) group, (ii) A is substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group and B is substituted at the 2-position with a nonpolar (NP) group and at the 5-position with a polar (P) group, or (iii) A is substituted at the 2-position with one of a polar (P) or nonpolar (NP) group and B is substituted at the 2-position with the other of a nonpolar (NP) or a polar (P) group;

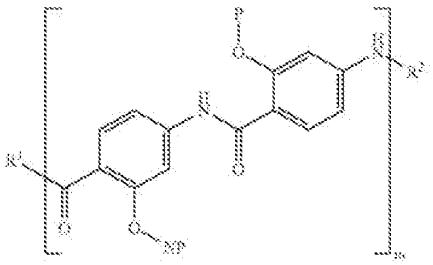
NP is a nonpolar group independently selected from R^5 or $—U—R^4$ wherein R^4 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

p is independently 0 to 8; and

m is 2 to at least about 500.

9. The polymer or oligomer of claim **8**, wherein said polymer or oligomer comprises a compound of formula XII

(XII)



wherein:

NP is a nonpolar group independently selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

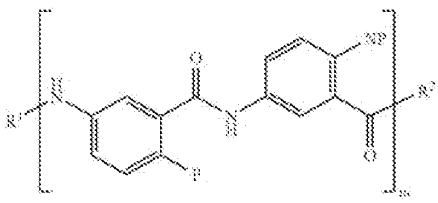
P is a polar group U—$(CH_2)_p$—V wherein U is selected from the group consisting of O, S, and no atom and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 30.

10. The polymer or oligomer of claim **8**, wherein said polymer or oligomer comprises a compound of formula XIV,

(XIV)



wherein:

NP is a nonpolar group independently selected from R^4 or —U—R^4 wherein R^4 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is selected from the group consisting of O, S, and no atom and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 30.

11. The polymer or oligomer of claim **1**, wherein:

x is NR^5, y is CO, and R^5 is hydrogen;

A and B are o-phenylene wherein A is substituted at the 5-position with a polar (P) group and B is substituted at the 5-position with a nonpolar (NP) group;

NP is a nonpolar group independently selected from R^4 or —U—R^4 wherein R^4 selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, iso-butyl, n-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

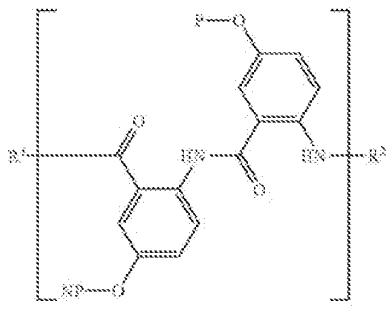
P is a polar group U—$(CH_2)_p$—V wherein U is selected from the group consisting of O, S, and no atom and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, pyridine, piperidine, piperazine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 500.

12. The polymer or oligomer of claim **11**, wherein said polymer or oligomer comprises a compound of formula XIII:

(XIII)



wherein:

NP is a nonpolar group independently selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

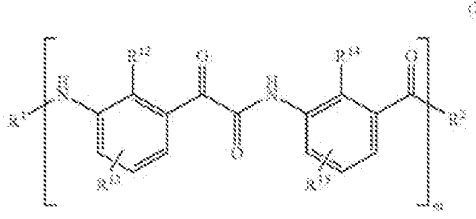
P is a polar group $(CH_2)_p$—V wherein V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, guanidine, piperazine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 30.

13. The polymer or oligomer of claim **11**, wherein said polymer or oligomer comprises a compound of formula XV:

(XV)



wherein

either R^{13} and R^{14} are independently polar (P) groups and R^{15} and R^{16} are independently nonpolar (NP) groups substituted at one of the remaining unsubstituted carbon atoms, or R^{13} and R^{14} are independently nonpolar (NP) groups and R^{15} and R^{16} are independently polar (P) groups;

NP is a nonpolar group independently selected from R^4 or —U—R^4 wherein R^4 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl,

iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U is defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is selected from the group consisting of O and S and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, guanidine, pyridine, piperazine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 30.

14. A polymer or oligomer comprising a compound of formula II

(II)

wherein:

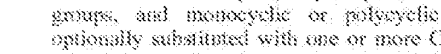
x and y can be (i) taken independently wherein x is NR^3, O, S, $(CR^7R^8)NR^3$, $(CR^7R^8)O$, or $(CR^7R^8)S$, y is C═O, C═S, O═S═O, —C(═O)C(═O)—, $(CR^5R^6)C$═O or $(CR^5R^6)C$═S, and R^3 is hydrogen, methyl or ethyl; or, (ii) taken together to be pyromellitic diimide; and R^5 and R^6 together are $(CH_2)_2NR^{1/2}(CH_2)_2$ and $R^{1/2}$ is selected from the group consisting of hydrogen, C(═N)CH_3 and C(═NH)—N2 and R^7 and R^8 together are $(CH_2)_p$ wherein p is as defined below;

both A and B are independently optionally substituted o-, m-, p-phenylene, or optionally substituted heteroarylene wherein (i) A and B are both substituted with a polar (P) group and a nonpolar (NP) group, (ii) one of A and B is substituted with a polar (P) group and a nonpolar (NP) group and the other of A and B is substituted with neither a polar nor a nonpolar group, or (iii) one of A or B is substituted with a polar (P) group and the other of A or B is substituted with a nonpolar (NP) group;

R^1 is (i) -y-B-y-R^2 and R^2 is -x-$(CH_2)_p$—W, wherein x is as defined above and W is hydrogen, phenyl optionally substituted with up to three substituents selected from the group consisting of halogen, C_1–C_4 alkyl, C_1–C_4 alkoxy, and carboxyl, N-maleimide, or V as defined below, and p is as defined below; or, (ii) R^1 and R^2 together are a single bond;

NP is a nonpolar group an independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from the group consisting of hydrogen, C_1–C_2 alkyl, C_1–C_6 haloalkyl, C_3–C_{18} branched alkyl, C_3–C_8 cycloalkyl, monocyclic or polycyclic phenyl optionally substituted with one or more C_1–C_4 alkyl, C_1–C_4 alkoxy or halo groups, and monocyclic or polycyclic heteroaryl optionally substituted with one or more C_1–C_4 alkyl, C_1–C_4 alkoxy, or halo groups, and U and p are as defined below;

P is a polar group selected from the group consisting of IIIa, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene.



(IIIa)

wherein,

U is absent or selected from the group consisting of O, S, S(═O), $S(═O)_2$, NH, —C(═O)O—, —C(═O)NH—, —C(═O)S—, —C(S)NH—, —$S(═O)_2$NH—, and C(═NO—) wherein groups with two chemically nonequivalent termini can adopt both possible orientations;

V is selected from the group consisting of amino, hydroxyl, thio, C_1–C_6 alkylamino, C_1–C_6 dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, C_1–C_8 alkoxycarbonyl, basic heterocycle, and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino;

and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino;

and the alkylene chain is optionally substituted with an amino or hydroxyl group or unsaturated;

p is independently 0 to 8; and

m is 2 to at least about 500.

15. The polymer or oligomer of claim **14**, wherein:

x═NH and y═CO;

A and B are m- or p-phenylene wherein (i) A is substituted at the 2-position with a polar (P) group and B is substituted at the 5-position with a nonpolar (NP) group, or (ii) A is substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group and B is either substituted at the 2- position with a nonpolar (NP) group and at the 5-position with a polar (P) group or B is unsubstituted;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, iso-butyl, sec-butyl, tert-butyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

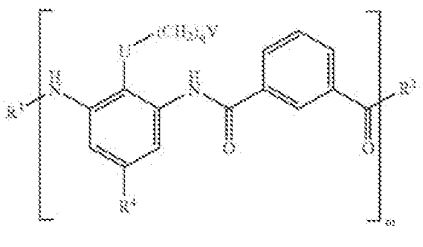
P is a polar group U—$(CH_2)_p$—V wherein U is absent or selected from the group consisting of O and S, and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, piperidine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 500.

16. The polymer or oligomer of claim **15**, where A is an optionally substituted 1,3-diaminobenzene and B is an optionally substituted iso-phthalic acid.

17. The polymer or oligomer of claim **15**, wherein said polymer or oligomer comprises a compound of formula XI



(XI)

wherein:

R^4 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl;

U is O or S;

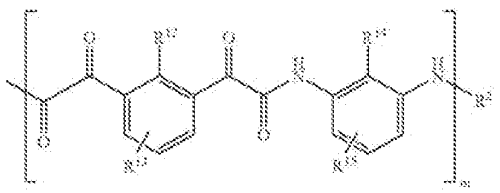
V is amino, lower alkyl amino, lower dialkylamino, or guanidine;

p is independently 0–8; and

m is 2 to at least about 30.

18. The polymer or oligomer of claim **15**, wherein said polymer or oligomer composes a compound of formula XVI

(XVI)



wherein:

either R^{12} and R^{14} are independently polar (P) groups and R^{13} and R^{15} are independently nonpolar (NP) groups substituted at one of the remaining unsubstituted carbon atoms, or R^{13} and R^{14} are independently nonpolar (NP) groups and R^{12} and R^{15} are independently polar (P) groups;

NP is a nonpolar group independently selected from R^4 or —U—R^4 where R^4 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U is as defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is absent or selected from the group consisting of O and S, and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, piperidine, and 4-alkylpiperazine;

U is O or S;

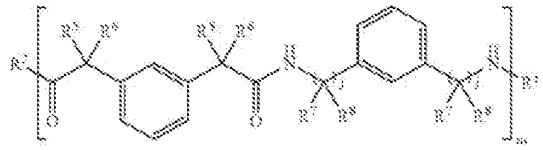
V is amino, lower alkyl amino, lower dialkylamino, or guanidine;

p is independently 0 to 8; and

m is 2 to at least about 30.

19. The polymer or oligomer of claim **15**, wherein said polymer or oligomer comprises a compound of formula XX

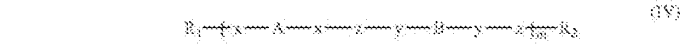
(XX)



wherein j is independently 0 or 1, R^5 and R^6 together are $(CH_2)_pNH(CH_2)_p$ and R^7 and R^8 together are $(CH_2)_p$ wherein p is 4 to 6.

20. A polymer or oligomer comprising a compound of formula IV

(IV)



wherein:

x is NR^3 or NHNH; y is NR^3, NHNH, S or O; and R^3 is hydrogen, methyl or ethyl;

z is C═O, —(C═O)C(═O)—, C═S or O═S═O;

A and B are independently optionally substituted o-, m-, p-phenylene or optionally substituted heteroarylene wherein (i) A and B are both substituted with a polar (P) group and a nonpolar (NP) group, (ii) one of A and B is substituted with a polar (P) group and a nonpolar (NP) group and the other of A and B is substituted with neither a polar nor a nonpolar group, (iii) one of A or B is substituted with one or two polar (P) group(s) and the other of A or B is substituted with one or two nonpolar (NP) group(s), or (iv) A is substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group and B is unsubstituted;

R^1 is (i) —B-y-R^3 and R^2 is -x-$(CH_2)_p$—W wherein x is as defined above and W is hydrogen, pyridine and phenyl said pyridine or phenyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, C_1–C_6 alkoxy, C_1–C_6 alkoxycarbonyl, and benzyloxycarbonyl; (ii) R^1 is H and R is -x-$(CH_2)_p$—V, or (iii) R^1 and R^2 together are a single bond;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from the group consisting of C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_3–C_{12} branched alkyl, C_3–C_8 cycloalkyl, monocyclic or polycyclic phenyl optionally substituted with one or more C_1–C_4 alkyl or halo groups, and monocyclic or polycyclic heteroaryl optionally substituted with one or more C_1–C_4 alkyl or halo groups, and U and p are as defined below;

P is a polar group selected from the group consisting of IIIa, hydroxyethoxymethyl, methoxyethoxymethyl and polyoxyethylene,

—U—$(CH_2)_p$—V (IIIa)

wherein:

U is absent or selected from the group consisting of O, S, S(═O), $S(═O)_2$, NH, —C(═O)O—, —C(═O)NH—, —C(═O)S—, —C(═S)NH—, —$S(═O)_2$NH—, and C(═NO—) wherein groups with two chemically nonequivalent termini can adopt both possible orientations;

V is selected from the group consisting of amino, hydroxyl, C_1–C_6 alkylamino, dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, basic heterocycle, and phenyl optionally substituted with an amino, C_1–C_6 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino;

and the alkylene chain is optionally substituted with an amino or hydroxyl group or optionally unsaturated;

p is independently 0 to 8; and

m is 2 to at least about 500.

21. The polymer or oligomer of claim **20**, wherein:

x and y are NR^3, z is C═O or C═S, and R^3 is hydrogen;

A and B are independently optionally substituted o-, m-, or p-phenylene;

NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from the group consisting of hydrogen, C_1–C_8 alkyl, C_3–C_{12} branched alkyl, C_3–C_8 cycloalkyl, phenyl optionally substituted with one or more C_1–C_4 alkyl groups and heteroaryl optionally substituted with one or more C_1–C_4 alkyl groups, and U and p are as defined below;

P is a polar group selected from the group consisting of IIIa, hydroxyethoxymethyl, methoxyethoxymethyl or polyoxyethylene,

—U—$(CH_2)_p$—V (IIIa)

wherein:

U is O, S, S(═O), $S(═O)_2$, NH, or absent;

V is selected from a group consisting of amino, hydroxyl, C_1–C_6 alkylamino, dialkylamino, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, amidine, guanidine, semicarbazone, and imidazole, piperidine, piperazine, 4-alkylpiperazine and phenyl optionally substituted with an amino, C_1–C_3 alkylamino, C_1–C_6 dialkylamino and lower acylamino optionally substituted with one or more amino, lower alkylamino or lower dialkylamino;

and the alkylene chain is optionally substituted with an amino or hydroxyl group;

p is independently 0 to 8; and,

m is 2 to at least about 500.

22. The polymer or oligomer of claim **20**, wherein:

x and y are NH, z is C=O;

A and B are m- or p-phenylene and either (i) A is substituted at the 2-position with a polar (P) group and B is substituted at the 5-position with a nonpolar (NP) group, or (ii) A is substituted at the 5-position with a polar (P) group and B is substituted at the 2-position with a nonpolar (NP) group, or (iii) A and B are both substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group, or (iv) A is substituted at the 2-position with a polar (P) group and at the 5-position with a nonpolar (NP) group and B is unsubstituted;

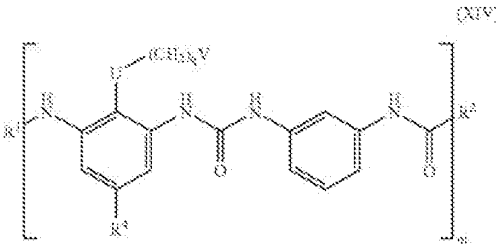
NP is a nonpolar group independently selected from R^4 or —U—$(CH_2)_p$—R^4 wherein R^4 is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, iso-propyl, iso-butyl, sec-butyl, tert-butyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is absent or selected from the group consisting of O and S and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 500.

23. The polymer or oligomer of claim **20**, wherein said polymer or oligomer comprises a compound of formula XIV



(XIV)

wherein:

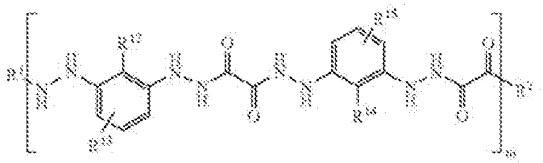
R^4 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

U is absent, O or S and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, and 4-alkylpiperazine;

p is 0 to 8; and

m is 2 to at least about 30.

24. The polymer or oligomer of claim **20**, wherein said polymer or oligomer comprises a compound of formula XVII



(XVII)

wherein:

either R^{12} and R^{14} are independently polar (P) groups and R^{13} and R^{15} are independently nonpolar (NP) groups substituted at one of the remaining unsubstituted carbon atoms, or R^{12} and R^{14} are independently nonpolar (NP) groups and R^{13} and R^{15} are independently polar (P) groups;

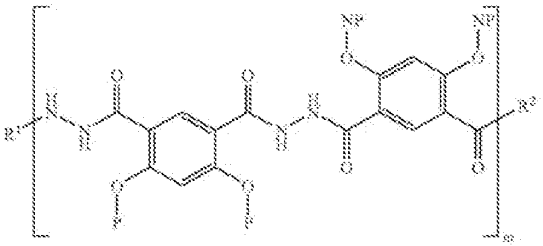
NP is a nonpolar group independently selected from R^4 or —U—R^4 wherein R^4 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, and sec-pentyl, and U and p are as defined below;

P is a polar group U—$(CH_2)_p$—V wherein U is selected from the group consisting of O and S and V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, guanidine, pyridine, piperazine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 30.

25. A polymer or oligomer comprising a compound of formula XVIII



(XVIII)

wherein:

x=NH and y=CO;

R^1 is (i) -y-C and R^2 is OH or NH_2 wherein C is selected from the group consisting of C_1–C_6 alkyl, C_1–C_6 haloalkyl, vinyl, 2-propenyl, H-x-$(CH_2)_p$—, (C_1–C_6-alkoxy)C(=O)$(CH_2)_p$—, C_1–C_6 alkoxy, benzyloxy, t-butoxy, pyridine and phenyl said pyridine or phenyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, C_1–C_6 alkoxy, C_1–C_6 alkoxycarbonyl, and benzyloxycarbonyl; or, (ii) is H and R^2 is -x-$(CH_2)_p$—W wherein x is as defined above and p is as defined below and W is N-maleimide or V as defined below, or (iii) -y-C and R^2 is x$(CH_2)_p$—W; or (iv) R^1 and R^2 together are a single bond;

NP is a nonpolar group independently selected from R^a or $—(CH_2)_p—R^a$ wherein R^a is selected from the group consisting of hydrogen methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, sec-pentyl, and C_1—C_3-haloalkyl, and p is as defined below;

P is a polar group $(CH_2)_p—V$ wherein V is selected from the group consisting of amino, lower alkyl amino, lower dialkylamino, imidazole, guanidine, $NH(CH_2)_pNH_2$, $N(CH_2CH_2NH_2)_2$, piperidine, piperazine, and 4-alkylpiperazine;

p is independently 0 to 8; and

m is 2 to at least about 30.

26. A method of killing microorganisms, said method comprising the steps of:

Providing a substrate having disposed thereon a contact killing, facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20**;

Placing said facially amphiphilic polymer or oligomer disposed thereon on said substrate in contact with a microorganism to allow formation of pores in the cell wall of said microorganism.

27. The method of claim **26**, wherein said substrate is selected from the group consisting of wood, synthetic polymers, plastics, natural and synthetic fibers, cloth, paper, rubber and glass.

28. The method of claim **27**, wherein said substrate is from a plastic selected from the group consisting of polysulfone, polyacrylate, polyurea, polyethersulfone, polyamide, polycarbonate, polyvinylidenefluoride, polyethylene, polypropylene and cellulosics.

29. A microbiocidal composition comprising a facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20** and a solid support selected from the group consisting of wood, synthetic polymers, natural and synthetic fibers, cloth, paper, rubber and glass.

30. The microbiocidal composition of claim **29**, wherein said solid support is a plastic selected from the group consisting of polysulfone, polyacrylate, polyethersulfone, polyamide, polycarbonate, polyvinylidenefluoride, polyethylene, polypropylene and cellulosics.

31. A method for identifying a facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20**, said method comprising:

(1) selecting a polymer or oligomer backbone or scaffold in which polar (P) and nonpolar (NP) groups can be incorporated;

(2) determining parameters for a molecular mechanics force field utilizing ab initio quantum mechanical calculations;

(3) calculating energetically accessible conformations of said backbone using molecular dynamics or molecular mechanics calculations;

(4) identifying energetically accessible conformations of said backbone wherein the periodicity of a geometrical/conformational repeat matches a sequence repeat;

(5) synthesizing monomers with polar and nonpolar substituents;

(6) synthesizing an antimicrobial polymer or oligomer containing said monomers by solution or solid-phase synthesis.

32. A process for producing an antimicrobial surface by attaching an antimicrobial facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20** to a surface, said process comprising treating said surface with a first chemically reactive group and reacting said polymer or oligomer linked to a second reactive group thereto.

33. The process of claim **32**, wherein said first reactive group is a 1-(trialkoxysilyl)propylamine and said second reactive group is an activated carboxylic acid.

34. The process of claim **32**, wherein said first reactive group is a ω-(trialkoxysilyl)alkyl bromomethylacetamide and said second reactive group is a thiol.

35. The process of claim **32**, wherein said first reactive group is a N-[ω-(trialkoxysilyl)alkyl] maleimide and said second reactive group is a thiol.

36. The process of claim **32**, wherein said first reactive group is a gold surface and said second reactive group is a thiol.

37. An antimicrobial composition comprising a facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20** and a composition selected from the group consisting of paint, coatings, lacquer, varnish, caulk, grout, adhesives, resins, films, cosmetics, soap and detergent.

38. An improved catheter, said improvement comprising incorporating or attaching an antimicrobial facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20** therein or thereto.

39. An improved contact lens, said improvement comprising incorporating or attaching an antimicrobial facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20** therein or thereto.

40. An improved plastic device for the hospital and laboratory, said improvement comprising incorporating or attaching an antimicrobial facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20** therein or thereto.

41. An improved woven and nonwoven fabric for hospital use, said improvement comprising incorporating or attaching an antimicrobial facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20** therein or thereto.

42. A microbiocidal composition comprising a facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20** and a medical device or medical product.

43. The microbiocidal composition of claim **42**, wherein the medical device or medical product is selected from the group consisting of surgical gloves, implanted devices, sutures, catheters, dialysis membranes, and water filters and implements.

44. A microbiocidal composition comprising a facially amphiphilic polymer or oligomer of claim **1**, claim **14**, or claim **20** and a material comprising spinnable fibers.

45. The microbiocial composition of claim **44**, wherein the material comprising spinnable fibers is selected from the group consisting of fabrics, surgical gowns, and carpets.

* * * * *

Exhibit 12

PolyMedix®

Revolutionizing the Treatment of Serious Infectious Diseases & Cardiovascular Disorders with Biomimetics

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Press Releases

PolyMedix Expands Research Science Advisory Board

Radnor, PA (November 23, 2010) - PolyMedix, Inc. (OTC BB: PYMX), an emerging biotechnology company focused on developing new therapeutic drugs to treat life-threatening infectious diseases and acute cardiovascular disorders, has expanded its advisory relationships through the development of its Scientific Advisory Board (SAB) focused on PolyMedix's basic scientific research. The SAB is comprised of world-renown scientists who will actively collaborate with PolyMedix to advance its preclinical portfolio of therapeutic drug candidates and PolyCide™ for biomaterials applications.

"We are honored to have the opportunity to work with such distinguished and accomplished scientific leaders," commented Dr. Richard Scott, Vice President of Research at PolyMedix. "Our advisors and scientific founders have been instrumental in guiding our research strategies and helping us develop our novel drug discovery programs. We look forward to their wisdom as we continue to discover innovative therapeutic drugs for important life-threatening infectious diseases and other disorders, particularly as we strive to develop next generations of our defensin-mimetic antibiotics for applications such as Gram-negative food-borne and fungal infections."

Members of the Scientific Advisory Board include:

William F. DeGrado, Ph.D.: Professor in the Department of Biochemistry & Biophysics in the School of Medicine, and an adjunct member of the Chemistry Department, at the University of Pennsylvania. Dr. DeGrado is one of the founders of PolyMedix's computational drug design technology that uses protein targets with well-understood physical structures and biological activity to design small molecule compounds that mimic or regulate the activity of these targets. He is a member of the National Academy of Science, and the American Academy of Arts and Sciences. Dr. DeGrado's research interests include: de novo protein and peptide design; peptide mimetics; structure, stability, and function of membrane proteins, including integrins and viral ion channels; design of biomimetic polymers; bioinorganic chemistry; and computational approaches to small molecule and protein design. He has over 250 publications and a multitude of patents. Dr. DeGrado received his Ph.D. in organic chemistry from the University of Chicago.

Gregory N. Tew, Ph.D.: Professor, Polymer Sciences and Engineering, at the University of Massachusetts. Dr. Tew is one of the original scientific founders of PolyMedix's technology. His research focuses on a number of topics including the design of simple, small synthetic oligomers that capture the biological activity of proteins, such as host defense peptides. He has successfully designed a number of molecular scaffolds that show potent broad spectrum antimicrobial activity and at the same time have minimal toxicity against mammalian cells. Dr. Tew is a founding member of the American Chemical Society Polymer Division, and a Fellow and member of the Defense Science Study Group. He has over 100 peer-reviewed publications and has received several prestigious scientific awards including the PECASE, which is one of the highest honors given by the U.S. federal government for young scientists. Dr. Tew received his Ph.D. in materials science from the University of Illinois.

Gill Diamond, Ph.D.: Associate Professor in the Department of Oral Biology at the University of Medicine and Dentistry of New Jersey. Dr. Diamond's expertise focuses on the role of antimicrobial peptides in host defense of the lung and the oral cavity, focusing on the activity of beta-defensins and cathelicidins in defense against bacterial infections. He has also been examining the potential applications of antimicrobial peptide mimetics for infections in the oral cavity. Dr. Diamond received his Ph.D. in genetics from the Hebrew University in Jerusalem.

Henry S. Heine, Ph.D.: Senior Scientist at Ordway Research Institute in New York. Dr. Heine is currently a member of the American Society of Microbiology and voting member of the CLSI Subcommittee on Veterinary Antimicrobial Susceptibility Testing. He is a former member of the White House Task force for WMD Medical Countermeasures (BARDA-Bio WG) and FDA-CDER Anti-Infective Drugs Advisory Committee. His research focuses on the development and testing of both in vitro and in vivo animal model systems for evaluation of therapeutics against many of the CDC select agent class A and B bacterial pathogens. In addition, Dr. Heine has designed and evaluated non-human primate trials and provided advice and support for meeting the FDA's "animal rule" as the regulatory path to indication approval. Dr. Heine received his Ph.D. in microbiology from the Uniform Services University Health Sciences in Maryland.

William J. Weiss, M.S.: Director of Pre-Clinical Services at the University of North Texas Health Science Center. Mr. Weiss' expertise encompasses the development and evaluation of animal models of infectious disease, pharmacokinetic and

pharmacodynamic analysis, evaluation of antibacterial agents, and the discovery and development of new antimicrobial, antiviral and antifungal agents. He has over 30 years of industry experience which includes Director of Drug Evaluation at Cumbre Pharmaceuticals Inc., and Group Leader in Infectious Disease Discovery Research at Wyeth Research, Lederle Laboratories and Schering-Plough. He has worked on numerous antibacterial programs including the development of the marketed products, Suprax, Zosyn and Tygacil. Mr. Weiss received his M.S. in microbiology from Fairleigh Dickinson University in New Jersey.

About PolyMedix, Inc.

PolyMedix is a publicly traded biotechnology company focused on the development of novel drugs for the treatment of serious infectious diseases and acute cardiovascular disorders. PolyMedix uses a rational drug design approach to create non-peptide small molecule drug candidates. PMX-30063, PolyMedix's lead antibiotic compound that is currently in Phase 2 clinical trials, is a small molecule that mimics human host-defense proteins and has a mechanism of action distinct from those of current antibiotic drugs, a mechanism which is intended to make bacterial resistance unlikely to develop. PolyMedix plans to develop this compound for serious systemic Staphylococcal infections, including methicillin resistant Staphylococcus aureus (MRSA). PMX-60056, PolyMedix's lead heptagonist compound, has completed four clinical trials and is being further developed to reverse the anticoagulant activity of both heparin and low molecular weight heparins. PolyMedix believes that PMX-60056 could potentially be a safer and easier to use anticoagulant reversing agent, with broader activity, than the currently approved therapy for reversing heparin. PolyMedix also plans to continue the development of its PolyCides®, polymeric formulations as antimicrobial biomaterials, which can be used as additives to paints, plastics, and textiles to create self-sterilizing products and surfaces. For more information, please visit our website at www.polymedix.com.

This press release contains forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 that involve risks, uncertainties and assumptions that could cause PolyMedix's actual results and experience to differ materially from anticipated results and expectations expressed in these forward looking statements. PolyMedix has in some cases identified forward-looking statements by using words such as "anticipates," "believes," "hopes," "estimates," "looks," "expects," "plans," "intends," "goal," "potential," "may," "suggest," and similar expressions. Among other factors that could cause actual results to differ materially from those expressed in forward-looking statements, PolyMedix's compounds may not successfully complete clinical testing, or be granted regulatory approval to be sold and marketed in the United States or elsewhere. A more complete description of these risk factors is included in PolyMedix's filings with the Securities and Exchange Commission. You should not place undue reliance on any forward-looking statements. PolyMedix undertakes no obligation to release publicly the results of any revisions to any such forward-looking statements that may be made to reflect events or circumstances after the date of this press release

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Exhibit 13

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
William F. DeGrado	Professor
eRA COMMONS USER NAME	
DEGRADOW	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Kalamazoo College, Kalamazoo, MI	B.S.	1975-77	Chemistry
University of Chicago, Chicago, IL	Ph.D.	1977-81	Organic Chemistry

A. Personal Statement

My research focuses on small molecule and protein design as an approach to understanding macromolecule structure and function. One primary research interest is in the de novo design, in which one designs proteins beginning from first principles. This approach critically tests our understanding of protein folding and function, while also laying the groundwork for the design of proteins and biomimetic polymers with properties unprecedented in nature. The de novo design of proteins has proven to be a useful approach for understanding the features in a protein sequence that cause them to fold into their unique three-dimensional structures. In addition, it has been possible to design functionally interesting proteins, which bind redox-active cofactors, DNA, and transition metals. Finally, this approach has been extended to the design of membrane-active proteins, including ion channels, antibiotics and fusogenic agents. I also study the structure and function of a number of pharmacologically interesting systems. My research group at the University of Pennsylvania is determining the structure of the M2 proton channel from influenza A virus, and its mode of inhibition by various channel-blocking drugs. In collaboration with Joel Bennett (Department of Medicine), we study the mechanism of signal transduction of integrins such as αIIβb3, with a particular focus on the role played by the membrane-spanning regions of this protein. We have developed small molecule mimics of integrins and the platelet collagen receptor, gpVI. Finally, our group developed a number of small molecule mimics of antimicrobial host defense proteins, which show considerable promise for treating antibiotic-resistant infections.

B. Positions and Honors

Professional Experience:

1981-1990 Research Chemist, CR&D, DuPont Company, Wilmington, DE
1990-1992 Research Leader, CR&D, DuPont Company, Wilmington, DE
1992-1994 Research Fellow, R&D, The DuPont Merck Pharmaceutical Company, Wilmington, DE
1994-1996 Senior Director, R&D, The DuPont Merck Pharmaceutical Company, Wilmington, DE
1996- Professor, Dept. of Biochemistry & Biophysics, University of Pennsylvania, Philadelphia, PA
2001-2004 President, The Protein Society

Visiting Positions:

1987 Sloan Visiting Lecturer of Chemistry, Dept. of Chemistry, Harvard University
1987-1989 Adjunct Professor, Department of Biophysics, Johns Hopkins Medical School
1991 Adjunct Professor, Departments of Biochemistry & Biophysics, University of Pennsylvania
1994 Wellcome Visiting Professor, Louisiana State University

Honors:

1988 du Vigneaud Award for Peptide Research
1989 Protein Society Young Investigator Award
1990 A. Naff Lecture, University of Kentucky
1991 Oncley Lecture, University of Michigan
1992 Eli Lilly Award in Biological Chemistry
1993 DuPont Merck Summit Award
1993 Denkewalter Lecture, Loyola University
1994 Fellow, American Association for the Advancement of Science

1998	Fellow, American Academy of Arts and Sciences
1999	Member, National Academy of Sciences (U.S.A.)
2003	Merrifield Award, (presented by the Peptide Society)
2008	Ralph F. Hirschmann Award in Peptide Chemistry (Presented by the American Chemical Society)
2009	Makineni Award (APS)

C. Seected Peer-Reviewed Publications (out of 300+ publications)

1. Scott, R. W., DeGrado, W. F. & Tew, G. N. (2008). De novo designed synthetic mimics
2. of antimicrobial peptides. *Curr Opin Biotechnol* 19, 620-7.
3. Caputo, G. A., Litvinov, R. I., Li, W., Bennett, J. S., DeGrado, W. F. & Yin, H. (2008). Computationally designed peptide inhibitors of protein-protein interactions in membranes. Biochemistry 47, 8600-6.
4. Shu, J. Y., Tan, C., DeGrado, W. F. & Xu, T. (2008). New design of helix bundle peptide-polymer conjugates. Biomacromolecules 9, 2111-7.
5. Moore, D. T., Berger, B. W. & DeGrado, W. F. (2008). Protein-protein interactions in the membrane: sequence, structural, and biological motifs. Structure 16, 991-1001.
6. Stouffer, A. L., Ma, C., Cristian, L., Ohigashi, Y., Lamb, R. A., Lear, J. D., Pinto, L. H. & DeGrado, W. F. (2008). The interplay of functional tuning, drug resistance, and thermodynamic stability in the evolution of the M2 proton channel from the influenza A virus. *Structure* **16**, 1067-76.
7. Basani, R. B., Zhu, H., Thornton, M. A., Soto, C. S., Degrado, W. F., Kowalska, M. A., Bennett, J. S. & Poncz, M. (2009). Species differences in small molecule binding to alpha IIb beta 3 are the result of sequence differences in 2 loops of the alpha IIb beta propeller. *Blood* **113**, 902-10.
8. Bell, C. B., Calhoun, J. R., Bobyr, E., Wei, P. P., Hedman, B., Hodgson, K. O., Degrado, W. F. & Solomon, E. I. (2009). Spectroscopic definition of the biferrous and biferric sites in de novo designed four-helix bundle DFsc peptides: implications for O2 reactivity of .binuclear non-heme iron enzymes. *Biochemistry* **48**, 59-73.
9. Bissonnette, M. L., Donald, J. E., DeGrado, W. F., Jardetzky, T. S. & Lamb, R. A. (2009). Functional analysis of the transmembrane domain in paramyxovirus F protein-mediated membrane fusion. *J Mol Biol* **386**, 14-36.
10. Choi, S., Isaacs, A., Clements, D., Liu, D., Kim, H., Scott, R. W., Winkler, J. D. & DeGrado, W. F. (2009). De novo design and in vivo activity of conformationally restrained antimicrobial arylamide foldamers. *Proc Natl Acad Sci U S A* **106**, 6968-73.
11. Khurana, E., Dal Peraro, M., DeVane, R., Vemparala, S., DeGrado, W. F. & Klein, M. L. (2009). Molecular dynamics calculations suggest a conduction mechanism for the M2 proton channel from influenza A virus. *Proc Natl Acad Sci U S A* **106**, 1069-74.
12. Kuroda, K., Caputo, G. A. & DeGrado, W. F. (2009). The role of hydrophobicity in the antimicrobial and hemolytic activities of polymethacrylate derivatives. *Chemistry* **15**, 1123-33.
13. Liu, F., Dumont, C., Zhu, Y., DeGrado, W. F., Gai, F. & Gruebele, M. (2009). A one-dimensional free energy surface does not account for two-probe folding kinetics of protein alpha(3)D. *J Chem Phys* **130**, 061101.
14. Miller, M. W., Basra, S., Kulp, D. W., Billings, P. C., Choi, S., Beavers, M. P., McCarty, O. J., Zou, Z., Kahn, M. L., Bennett, J. S. & DeGrado, W. F. (2009). Small-molecule inhibitors of integrin alpha2beta1 that prevent pathological thrombus formation via an allosteric mechanism. *Proc Natl Acad Sci U S A* **106**, 719-24.
15. Tang, J., Yin, H., Qiu, J., Tucker, M. J., DeGrado, W. F. & Gai, F. (2009). Using two fluorescent probes to dissect the binding, insertion, and dimerization kinetics of a model membrane peptide. *J Am Chem Soc* **131**, 3816-7.

Exhibit 14

Dr. Michael L. Klein

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fax: 215-204-1532
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Theory / Simulation / Modeling

Appointments
2009-Director, TempleInstitute for Computational Molecular Science
2009-Carnell Professor, College of Science & Technology, Temple University
1994-2009 Director, Penn Center for Molecular Modeling
1993-2009 Director, Laboratory for Research on the Structure of Matter
1993-2009 Hepburn Professor of Physical Science, University of Pennsylvania
1987- Professor of Chemistry, University of Pennsylvania
1968-87 Associate, Senior, & Principal Research Officer,
Chemistry Division, NRCC, Ottawa, Canada

Awards and Honors
2009 National Academy of Sciences
2008 American Chemical Society – *Peter Debye Award in Physical Chemistry*
2008 University of Oxford – *Hinshelwood Lecturer*
2008 Honorary Fellow, Chemical Research Society of India
2006 Chemical Research Society of India – *CNR Rao Award*
2005 Honorary Fellow, Indian Academy of Sciences – Bangalore
2005 Honorary Member, Materials Research Society of India
2004 European Physical Society, CECAM Prize for Computational Science
2004 Associate of TWAS, Academy of Sciences of the Developing World
2003 Fellow, Royal Society of London
2003 Fellow, American Academy of Arts & Sciences
2003 Fellow, Institute of Physics UK
2003 Schlumberger Professor, Universities of Oxford & Cambridge, UK
1999 American Physical Society, Aneesur Rahman Prize Computational Physics
1998 American Chemical Society, Philadelphia Section Award
1998 Linnett Professorship, University of Cambridge, UK
1998 Honorary Fellow Sydney Sussex College, Cambridge, UK
1997 Miller Professorship, University of California, Berkeley
1996 Alexander von Humboldt Award, Max-Planck-Institute, Stuttgart
1993 Hepburn Professor of Physical Science, University of Pennsylvania
1991-93 William Smith Professor of Chemistry, University of Pennsylvania

1991 Fellow American Physical Society
1989 Guggenheim Fellow
1988 Néel Professor, École Normale Supérieure, Lyon, France
1985 Fellow Commoner, Trinity College Cambridge, UK
1984 Fellow Royal Society of Canada

Publications: 570 papers and 4 books (Edited)

Reports:
Cyberinfrastructure NSF Blue Ribbon Panel (2001-2003; D. Atkins, Chair)
www.communitytechnology.org/nsf_ci_report/
Chemistry at the Centre International Review UK Chemical Sciences (2002; G. Whitesides, Chair)
http://www.epsrc.ac.uk/AboutEPSRC/IntRevs/2002ChemIR.htm
New Science for a Sustainable & Secure Energy Future (2008; BESAC sub-committee report)
http://www.er.doe.gov/bes/reports/files/NSSSEF_rpt.pdf
Chemistry for the Next Decade International Review UK Chemical Research (2009; M.L. Klein, Chair)
http://www.epsrc.ac.uk/AboutEPSRC/IntRevs/2009Chemistry/townmeeting.htm
see also: http://www.rsc.org/Education/EiC/issues/2009July/Endpoint.asp

Selected Publications
"Quantum character of a proton in a hydrogen bond" M.E. Tuckerman, D. Marx, M.L. Klein, M. Parrinello, *Science* 275, 817-820 (1997).

"Assessment of all-atom potentials for modeling membranes: MD simulations of solid & liquid alkanes and crystals of phospholipid fragments" D.J. Tobias, K. Tu, M.L.Klein, *J. Chem Phys.* 94, 1482-1502 (1997).

"Molecular dynamics simulation of a synthetic ion channel" Q. Zhong, Q. Jiang, P.B. Moore, D.M. Newns, M.L.Klein, *Biophys J.* 74, 3-10 (1998).

"Molecular dynamics study of the LS3 voltage-gated ion channel" Q. Zhong, P.B. Moore, D.M. Newns, M.L.Klein, *FEBS Lett.* 427, 267-270 (1998).

"Molecular dynamics simulations of the influenza a virus M2 ion channel in a membrane-mimetic environment" Q. Zhong, T. Husslein, D. Newns, M L.Klein, *FEBS Letters* 434, 265-271 (1998).

"Molecular dynamics simulation of a synthetic four-α-helix bundle that binds the anesthetic halothane" L.A. Davis, M.L. Klein, D. Scharf, *FEBS Lett.* 455, 332-338 (1999).

"Molecular dynamics simulations of supported phospholipid/alkanethiol bilayers on a Gold(111) surface" M. Tarek, K. Tu, M.L. Klein, D.J. Tobias, *Biophys. J.* 77, 964-972 (1999).

"Molecular dynamics study of lipid-DNA complexes" S. Bandyopadhyay, M. Tarek and M.L.

Klein, *J. Phys. Chem. B* 103, 10075-10080 (1999).

"Molecular dynamics simulation of four-a-helix bundles that bind the anesthetic halothane" L.A. Davies, Q. Zhong, M.L Klein, D. Scharf, *FEBS Letters* 478, 61-66 (2000).

"Two possible conducting states of the influenza a virus M2 ion channel" Q. Zhong, D.M. Newns, P. Pattnaik, J.D. Lear, M.L. Klein, *FEBS Letters* 473, 195-198 (2000).

"Molecular dynamics study of structure and gating of low molecular weight ion channels" D.M. Newns, Q. Zhong, P. B. Moore, T. Husslein, P. Pattnaik, M.L. Klein, *Parallel Computing* 26, 965-976 (2000).

"Water on the move" M.L. Klein, *Science* 291, 2106 (2001).

"Electrostatic interactions in a neutral model phospholipid bilayer with highly unsaturated alkyl chains by molecular dynamics simulations" L. Saiz, M.L. Klein, J. Chem. Phys. 116, 3052-3057 (2002).

"Histidine protonation in aqueous solution via constrained Car-Parrinello molecular dynamics" I. Ivanov, M.L.Klein, *J. Am. Chem. Soc.* 124, 13380-13381 (2002).

"Influence of anesthetic and nonimmobilizer molecules on the physical properties of a polyunsaturated lipid bilayer" L. Koubi, L. Saiz, M. Tarek, D. Scharf, M.L. Klein, *J. Phys. Chem. B.* 107, 14500-14508 (2003).

"Characterization of the dizinc analogue of the synthetic diiron protein DF1 using ab initio and hybrid quantum/classical molecular dynamics simulations" A. Magistrato, W.F. DeGrado, A. Laio, U. Rothlisberger, J. VandeVondele, M.L.Klein, *J. Phys. Chem. B* 107, 4182-4188 (2003).

"Probing the configurational space of a metalloprotein core: An ab initio molecular dynamics study of Duo Ferro 1 Binuclear Zn Cofactor" G.A. Papoian, W. F. DeGrado, M.L.Klein, *J. Am. Chem. Soc.* 125, 560-569 (2003).

"Transmembrane peptide-induced lipid sorting and mechanism of Lx-to-inverted phase transition using coarse grain molecular dynamics" S.O. Nielsen, C.F. Lopez, I. Ivanov, P.B. Moore, J.C. Shelley, M.L.Klein *Biophys. J.* 87, 2107-2115 (2004).

"Controlling the conformation of arylamides: computational studies of intramolecular hydrogen bonds between amides and ethers or thioethers" R.J. Doerksen, B. Chen, D.Liu, G.N. Tew, W.F. DeGrado, M.L.Klein, *Chem. Eur. J.* 10, 5008-5016 (2004).

"Computational approaches to nanobiotechnology: probing the interaction of synthetic molecules with phospholipid bilayers via a coarse grain model" G. Srinivas, M.L.Klein, *Nanotechnology* 15, 1289-1295 (2004).

"Hydrogen bonding structure and dynamics of water at the dimyristoylphosphatidylcholine lipid

bilayer surface from a molecular dynamics simulation" C.F. Lopez, S.O. Nielsen, M.L.Klein, P.B. Moore, *J. Phys. Chem. B.* 108, 6603-6610 (2004).

"Understanding nature's design for a nanosyringe" C. F. Lopez, S. O. Nielsen, P. B. Moore, M.L. Klein, *Proc. Natl. Acad. Sci. USA* 101, 4431-4434 (2004)

"Membrane bound hydraphiles facilitate cation translocation" G. Srinivas, C.F. Lopez, M.L. Klein, *J. Phys. Chem. B.* 108, 4231-4235 (2004).

"Effect of the pore region of a transmembrane ion channel on the physical properties of a simple membrane" L. Saiz, S. Bandyopadhyay, M.L.Klein, *J. Phys. Chem. B.* 108, 2608-2613 (2004).

"The transmembrane domain of the acetylcholine receptor: Insights from simulations on synthetic peptide models" L. Saiz, M.L.Klein, *Biophys. J.* 88, 959-970 (2005).

"Concentration effects of volatile anesthetics on the properties of model membrane: a coarse grain approach" M. Pickholz, L. Saiz, M.L.Klein, *Biophys. J.* 88, 1524-1534 (2005).

"Structure and dynamics of model pore insertion into a membrane" C.F. Lopez, S.O. Nielsen, B. Ensing, P.B. Moore, M.L.Klein, *Biophysical J.* 88, 3083-3094 (2005).

"Dynamical flexibility and proton transfer in the arginase active site probed by ab initio molecular dynamics" I. Ivanov, M.L. Klein, *J. Am. Chem. Soc.* 127, 4010-4020 (2005).
"Molecular dynamics simulations of surfactant self-organization at a solid-liquid interface" G. Srinivas, S.O. Nielsen, P. B. Moore, M.L. Klein, *J. Am. Chem. Soc.* 128, 848-853 (2006).

"Ab initio calculations of intramolecular parameters for a class of arylamide polymers" S. Vemparala, I. Ivanov, V. Pophristic, K. Spiegel, M.L. Klein, *J. Comput. Chem.* 27, 693-700 (2006).

"Controlling the shape and flexibility of arylamides: a combined ab initio, ab initio molecular dynamics and classical molecular dynamics study" V. Pophristic, S. Vemparala, I. Ivanov, Z. Liu, M.L. Klein, W.F. DeGrado, *J. Phys. Chem. B* 110, 3517-3526 (2006).

"Characterization of nonbiological antimicrobial polymers in aqueous solution and at water-lipid interfaces from all-atom molecular dynamics" I. Ivanov, S. Vemparala, V. Pophristic, K. Kuroda, W.F. DeGrado, J. A. McCammon, M.L. Klein, *J. Am. Chem. Soc.* 128, 1778-1779 (2006).

"Role of aromatic localisation in the gating process of a potassium channel" C. Domene, S. Vemparala, M.L. Klein, C. Venien-Bryan, D.A. Doyle, *Biophys. J.* 90, L01-L03 (2006).

"Metadynamics as a tool for exploring free energy landscapes of chemical reactions" B. Ensing, M. De Vivo, Z. Liu, P. Moore and M.L.Klein, *Acc. Chem. Res.* 39, 73-81 (2006).

"Probing membrane insertion activity of antimicrobial polymers via coarse-grain molecular dynamics" C.F. Lopez, S.O. Nielsen, G. Srinivas, W.F. DeGrado, M.L.Klein, *J. Chem. Theory*

and Comput. 2, 649-655 (2006).

"Shrinkage of a rapidly growing tumor by drug-loaded polymersomes: ph-triggered release through copolymer degradation" F. Ahmed, R. I. Pakunlu, G. Srinivas, A. Brannan, F. Bates, M.L.Klein, T. Minko, D.E. Discher, *Molecular Pharmaceutics* 3, 340-350 (2006).

"Self-assembling cyclic peptides: molecular dynamics studies of dimers in polar and nonpolar solvents" E. Khurana, S. O. Nielsen, B. Ensing, M.L.Klein, *J. Phys. Chem. B* 110, 18965-18972 (2006).

"Exploring the gating mechanism in the ClC chloride channel via metadynamics" F.L. Gervasio, M. Parrinello, M. Ceccarelli, M.L.Klein, *J. Mol. Biol.* 361, 390-398 (2006).

"Partitioning of anesthetics into a lipid bilayer and their interaction with membrane-bound peptide bundles" S. Vemparala, L. Saiz, R.G. Eckenhoff , M.L.Klein, *Biophys J. BioFAST* , (2006).

"Relative pK(a) values from first-principles molecular dynamics: the case of histidine deprotonation" I. Ivanov, B. Chen, S. Raugei, and M.L.Klein, *J. Phys. Chem B* 110, 6365-6371 (2006).

"Gemini surfactants at the air/water interface: a fully atomistic molecular dynamics study" E. Khurana, S.O. Nielsen and M.L.Klein, *J. Phys. Chem. B* 110, 22136-22142 (2006).

"Reorganization free energies for long-range electron transfer in a porphyrin-binding four-helix bundle protein" J. Blumberger, M L. Klein, *J. Am. Chem. Soc.* , ASAP article (2006).
"Polarization effects and charge transfer in the KcsA potassium channel" D. Bucher, S. Raugei, L. Guidoni, M. DalPeraro, U. Rothlisberger, P. Carloni, M.L.Klein, *Biophys. Chem.* 124, 292-301 (2006).

"Proton shuttles and phosphatase activity in soluble epoxide hydrolase" M. De Vivo, B. Ensing, M. Dal Peraro, G.A. Gomez, D.W. Christianson, M.L.Klein, *J. Am. Chem. Soc.* 129, 387-394 (2007).

"Modeling the charge distribution at metal sites in proteins for molecular dynamics simulations" M. Dal Peraro, K. Spiegel, G. Lamoureux, M. De Vivo, W.F. DeGrado, M.L. Klein, *J. Struct. Biol.* 157, 444-453 (2007).

"Role of zinc content on the catalytic efficiency of b1 metallo β-lactamases" M. Dal Peraro, A. J. Vila, P. Carloni, M.L.Klein, *J. Am. Chem. Soc.* 129, 2808-2816 (2007).

"Multi-property fitting and parameterization of a coarse grained model for aqueous surfactants" W. Shinoda, R. DeVane, M.L.Klein, *Mol. Sim.* 33, 27-36 (2007).

"A stable water chain in the hydrophobic pore of the amtb ammonium transporter" G.

Lamoureux, M.L.Klein, S. Bernèche, *Biophys. J.* 92, L82-L84 (2007).

"Emerging applications of polymersomes in delivery: From molecular dynamics to shrinkage of tumors," Discher DE, Ortiz V, Srinivas G, et al. *Progress in Polymer Science* 32 (8-9): 838-857 (2007)

"Azole-bridged diplatinum anticancer compounds. Modulating DNA flexibility to escape repair mechanism and avoid cross resistance," Spiegel K, Magistrato A, Carloni P, et al. *Journal of Phys. Chem.*B 111 (41): 11873-11876 (2007)

"Large-scale molecular dynamics simulations of self-assembling systems," Klein ML, Shinoda W
Science 321(5890): 798-800 (2008)

"Solution NMR structure of a designed metalloprotein and complementary molecular dynamics refinement" J.R. Calhoun, W. Liu, K. Spiegel, M. DalPeraro, M.L.Klein, K.G. Valentine, A.J. Wand, W.F. DeGrado, *Structure* 16, 210-215 (2008).

"Probing the structure of DNA carbon nanotube hybrids with molecular dynamics" R.R. Johnson, A.T. Johnson, M.L.Klein, *Nano Letters* 8, 69-75 (2008).

"Parameterization of azole-bridged dinuclear platinum anticancer drugs via a QM/MM force matching procedure" K. Spiegel, A. Magistrato, P. Maurer, P. Ruggerone, U. Rothlisberger, P. Carloni, J. Reedijk, M.L.Klein, *J Computational Chemistry* 29, 38-49 (2008).
"Coarse-grained molecular modeling of non-ionic surfactant self-assembly,"
Shinoda W, DeVane R, Klein ML *Soft Matter* 4 (12): 2454-2462 (2008)

"Probing Peptide Nanotube Self-Assembly at a Liquid-Liquid Interface with Coarse-Grained Molecular Dynamics," Khurana E, DeVane RH, Kohlmeyer A, et al. *Nano Letters* 8 (11): 3626-3630 (2008)

"Embedded cholesterol in the nicotinic acetylcholine receptor," Brannigan G, Henin J, Law R, et al. *Proceedings National Academy of Sciences* USA 105 (38): 14418-14423 (2008)

"Phosphodiester cleavage in ribonuclease H occurs via an associative two-metal-aided catalytic mechanism," De Vivo M, Dal Peraro M, Klein ML *Journal of the American Chemical Society* 130 (33): 10955-10962 (2008)

"X-ray diffraction and computation yield the structure of alkanethiols on gold(111),"
Cossaro A, Mazzarello R, Rousseau R, et al. *Science* 321 (5891): 943-946 (2008)

"Conformational changes and gating at the selectivity filter of potassium channels," Domene C, Klein ML, Branduardi D, et al. *Journal of the American Chemical Society* 130 (29): 9474-9480 (2008)

"United-Atom Acyl Chains For CHARMM Phospholipids," Henin J, Shinoda W, Klein ML

Journal of Physical Chemistry B 112 (23): 7008-7015 (2008)

"The role of conformation in ion permeation in a K+ channel," Domene C, Vemparala S, Furini S, et al. *Journal of the American Chemical Society* 130 (11): 3389-3398 (2008)

"Solution NMR structure of a designed metalloprotein and complementary molecular dynamics refinement," Calhoun JR, Liu W, Spiegel K, et al. *Structure* 16 (2): 210-215 (2008)

"Probing the structure of DNA-carbon nanotube hybrids with molecular dynamics," Johnson RR, Johnson ATC, Klein ML *Nano Letters* 8 (1): 69-75 (2008)

"Identification of a fluorescent general anesthetic, 1-aminoanthracene," Butts CA, Xi J, Brannigan G, et al. *Proceedings National Academy of Sciences* USA 106 (16): 6501-6506 (2009)

"Initial Response of the Potassium Channel Voltage Sensor to a Transmembrane Potential," Treptow W, Tarek M, Klein ML *Journal of the American Chemical Society* 131 (6): 2107- (2009)

"Evaluation of Electronic Coupling in Transition-Metal Systems Using DFT: Application to the Hexa-Aquo Ferric-Ferrous Redox Couple," Migliore A, Sit PHL, Klein ML *J. Chemical Theory and Computation* 5 (2): 307-323 (2009)

"Free Energy Landscape of a DNA-Carbon Nanotube Hybrid Using Replica Exchange Molecular Dynamics," Johnson RR, Kohlmeyer A, Johnson ATC, et al. *Nano Letters* 9 (2): 537-541(2009)

"Molecular dynamics calculations suggest a conduction mechanism for the M2 proton channel from influenza A virus," Khurana E, Dal Peraro M, DeVane R, et al. *Proceedings National Academy of Sciences* USA 106 (4): 1069-1074 (2009)

Exhibit 15

CURRICULUM VITAE

Gregory N. Tew

Polymer Science and Engineering Department
University of Massachusetts – Amherst
120 Governors Drive, Conte A617
Amherst, MA 01003
Tel: (413) 577-1612
Fax: (413) 545-0082
e-mail: tew@mail.pse.umass.edu

Personal:

Born: February 11, 1971; Married to Dawn C. Tew since 1996
Home: 6 Crestview Drive/P.O. Box 108, South Deerfield, MA

Education:

University of Pennsylvania, The Medical School — 2000-2001
Post-doctoral Fellow
Research Advisor: Prof. William F. DeGrado

University of Illinois at Urbana-Champaign — 1995-2000
Ph.D., Materials Chemistry
Research Advisor: Prof. Samuel I. Stupp
Thesis: "Phenylene Vinylene Based Supramolecular Materials"

North Carolina State University — 1989-1995
B.S., Chemistry, *Magna Cum Laude*
Research Advisor: Prof. David A. Shultz

Professional Positions:

University of Massachusetts – Amherst — 2007
Associate Professor, Polymer Science and Engineering

University of Massachusetts – Amherst — 2001-2007
Assistant Professor, Polymer Science and Engineering

University of Pennsylvania, The Medical School — 2000-2001
Post-doctoral Fellow

University of Illinois at Urbana-Champaign — 1995-2000
Research and Teaching Assistant

Burroughs-Wellcome, Co. — 1992-1995
Research Chemist, Organic Division

Societies:

American Chemical Society: Division of Organic Chemistry and Division of Polymers
Materials Research Society
American Association for the Advancement of Science

Principal Research Interests:

Supramolecular polymer science, directed self-assembly, bioinspired and biomimetic structures, self organization, well-defined macromolecular architectures, metal-containing polymers, membrane biophysics, physical organic chemistry, sensors, novel biomaterials, hydrogels

Awards & Honors:

2007:	American Chemical Society Polymer Division Herman F. Mark Young Scholar Award
2006:	IUPAC MACRO International Samsung Young Polymer Scientist Award
2005-2006:	Selected member of NSF-MEXT U.S.-Japan Young Faculty Exchange in BioNanoTechnology
2005-2010:	National Science Foundation CAREER Award Presidential Early Career
2004-2009:	Award for Scientists and Engineers (PECASE)
2004-2007:	DuPont Young Faculty Grant
2003-2006:	Office of Naval Research Young Investigator
2002-2005:	Army Research Office Young Investigator
2002-2005:	3M Untenured Faculty Award
1998-1999:	American Chemical Society-Division of Organic Chemistry Graduate Fellowship
1997-1998:	Beckman Institute for Advanced Science and Technology Research Fellowship
1997-1998:	R. C. Fuson Award for Outstanding Graduate Research
1995-1996:	Graduate Research Fellowship
1994-1995:	Hypercube Scholar – Outstanding Academic Senior
1993-1994:	Robert Proctor Undergraduate Research Scholarship
1993:	Outstanding Undergraduate Travel Award - American Chemical Society

LIST OF PUBLICATIONS

(*indicates I am the corresponding author)

-Publication Statistics-

1. Refereed Journal Articles – 114
2. Refereed Articles Published since joining UMass-PSE –107 (*7-submitted or in press, 5-in preparation*)
3. Patents – 3
4. Refereed or Invited Book Chapters – 9

Peer Reviewed:

At Umass-Amherst

In preparation

114. K. Lienkamp, A. E. Madkour, G. N. Tew, "Oligomeric and Polymeric Synthetic Mimics of Antimicrobial Peptides," in preparation, (2009).

113. R. R. .Maddikeri, Y. Zha, J. Jiang, S. P. Gido, G. N. Tew, "Magnetic Properties of Ferrocene and Mono Cobalt Functionalized Oxanorbornene Block Copolymers," in preparation, (2009).

112. R. R. Maddikeri, Y. Zha, J, Jiang, S. P. Gido, G. N. Tew, "Effect of Morphology on the Magnetic Properties of Cobalt Functionalized Oxanorbornene Block Copolymers," in preparation, (2009).

111. Z. M. AL-Badri, P. Dobriyal, R. Shunmugam, T. P. Russell, G. N. Tew, "Ferromagnetic Materials via Directed Self-Assembly", *Science*, in preparation, (2009).

Submitted

110. *H. Tang, L. Arnt, G. N. Tew, J. A. Finlay, L. Arnt, M. E. Callow, J. A. Callow, C. Hellio, T. Clare, "Activity of Host Defense Peptide Mimics Against Marine Fouling Organisms," *Journal of Peptide Science*, submitted, (2009).

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2. D. A. Shultz, G. N. Tew: "Electrochemical Oxidation of a Galvinol-Substituted Alkanethiol," *J. Org. Chem.* **59**, 6159-6160 (1994).

1. D. A. Shultz, D. A. Knox, L. W. Morgan, K. Sandberg, G. N. Tew: "Preparation of *meso*-Tetra(4-galvinolphenyl)porphyrin-A Building Block for Molecular Magnetic Materials," *Tetrahedron Lett.* **34**, 25, 3975-3977 (1993).

Peer Reviewed Articles Highlighted on the Cover or as a Frontispiece

1. *S. H. Seo, J-Y. Chang, G. N. Tew, "Self-Assembled Vesicles from an Amphiphilic *ortho*-Phenylene Ethynylene Macrocycle," *Angew. Chem. Int. Ed.*, **45**, 7526-7530, (2006). Highlighted with frontispiece.

2. *T. Kim, L. Arnt, E. Atkins, G. N. Tew, "Self-Assembled Structures with Liquid Crystalline Order in Aqueous Solution by Patterning *Meta*-Poly(phenylene ethynylene)s," *Chem: Eur. J.*, **12**, 2423-2427, (2006). Highlighted with frontispiece.

3. *G. N. Tew, N. Sanabria-DeLong, S. K. Agrawal, S. R. Bhatia, "New Properties from PLA-PEO-PLA Hydrogels", *Soft Matter*, **1**, 253-258, (2005). **Invited article*, Highlighted on the Cover.

4. *L. Arnt, K. Nüsslein, G. N. Tew, "Non-Hemolytic Abiotic Mimics of Host Defense Peptide Based on Phenylene Ethynylene," *J. Polym. Sci., Polym. Chem.*, **42**, 3860-3864, (2004). Highlighted on the Cover.

5. D. A. Harrington, H. Benna, G. N. Tew, R. C. Claussen, S. I. Stupp, "Supramolecular Fluorophores for Biological Studies: Phenylene Vinylene - Amino Acid Amphiphiles," *Chem. Bio.*, **12**, 1085-1091, (2005). Highlighted on the Cover.

JOURNAL NAME	IMPACT FACTOR	REFERENCE (Vol, Pg Nm, Yr)	TIMES CITED

Advanced Functional Materials	6.77	**15**, 1745-1750 (2005)	12
		19, 689-695 (2009)	0
Angewandte Chemie International Edition	10.232	**39**, 517-521 (2000)	67
		39, 1486-1489 (2000)	34
		45, 7526-7530 (2006)	25
Antimic. Agents Chemo.		**51**, 4125-4132 (2007)	11
Biochimica et. Bio Physica. Acta-Biomembranes	4.224	**1758**, 1387-1392 (2006)	23
Biomacromolecules	3.664	**4**, 193-195 (2003)	9
		9, 2784-2791 (2008)	1
		9, 2805-2810 (2008)	1
		9, 2980-2983 (2008)	2
		10, 353-359 (2009)	0
Biomaterials	5.196	**25**, 1087-1093 (2004)	39
Biopolymers		**90**, 83-93 (2008)	8
Chemistry and Biology	6.677	**12**, 1085-1091 (2005)	4
		13, 427-435 (2006)	16
Chem. Comm.	4.521	**12**, 1537-1539 (2005)	22
Chem: Eur. J.	5.015	**10**, 5008-5016 (2004)	20
		12, 2423-2427 (2006)	6
		14, 3904-3907 (2008)	10
		14, 5409-5412 (2008)	3
		15, 433-439 (2009)	2
Chem Mater.	5.104	**15**, 1249-1255 (2003)	23
Cur. Opin. BioTech		**19**, 620-627 (2008)	4
J. Am. Chem. Soc.	7.696	**120**, 5601-5602 (1998)	45
		121, 9852-9866 (1999)	76
		124, 7664-7665 (2002)	73

		126, 15870-15875 (2004)	57
		127, 13567-13572 (2005)	32
		127, 17235-17240 (2005)	18
		128, 2711-2714 (2006)	20
		128, 9264-9265 (2006)	26
		128, 13123-13129 (2006)	27
		129, 12141-12147 (2007)	19
		130, 2372-2372 (2008)	0
		130, 9836-9843 (2008)	8
		130, 10338-10344 (2008)	5
J. Controlled Rel.	4.012	**112**, 64-71 (2006)	25
J. Industrial Microbiol. Biotechnol.	1.416	**32**, 296-300 (2005)	17
J. Mat. Res.		**21**, 2118-2125 (2006)	8
J. Org. Chem.	3.790	**59**, 6159-6160 (1994)	11
		60, 3578-3579 (1995)	25
		68, 8780-8785 (2003)	31
		72, 342-347 (2007)	7
J. Phys. Chem. B.	4.115	**110**, 3527-3532 (2006)	17
		112, 3495-3502 (2008)	7
		113, 11179-11185 (2009)	0
J. Polm. Sci, Polym. Chem.	3.405	**42**, 3860-3864 (2004)	47
		43, 5831-5843 (2005)	31
		45, 1109-1121 (2007)	11
		45, 2601-2608 (2007)	6
		45, 5618-5625 (2007)	9
		46, 2640-2648 (2008)	9
		46, 6672-6676 (2008)	7
		47, 1266-1273 (2009)	2
		47, 3949-3956 (2009)	0
Langmuir	3.902	**19**, 2404-2408 (2003)	37
		23, 5039-5044 (2007)	10
		24, 12489-12495 (2008)	2
		24, 13148-13154 (2008)	1

		25, 1060-1067 (2009)	0
Macromolecules	4.277	**35**, 6090-6093 (2002)	47
		37, 1283-1288 (2004)	31
		37, 1163-1165 (2004)	22
		37, 1990-1993 (2004)	31
		38, 104-109 (2005)	28
		39, 1308-1310 (2006)	11
		39, 8283-8292 (2006)	10
		40, 2737-2744 (2007)	13
		40, 7864-7873 (2007)	5
		41, 1774-1784 (2008)	7
		41, 2022-2029 (2008)	6
		41, 4173-4179 (2008)	2
		41, 8436-8440 (2008)	5
		42, 6716-6722 (2009)	0
Macromol. Chem. Phys.		**209**, 516-524 (2008)	9
Macrol. Rapid Comm.		**29**, 1355-1362 (2008)	3
Mat. Sci. Eng. Reports		**57**, 28-64 (2007)	24
Microbiology-SGM	3.139	**152**, 1913-1918 (2006)	5
Mol. Cryst. Liq. Cryst.	.478	**305**, 303-307 (1997)	21
		317, 1-1 (1998)	0
MRS Bulletin	5.671	**25**, 42-48 (2000)	35
New J. Chem.		**32**, 670-675 (2008)	2
		32, 676-679 (2008)	5
Org. Lett.	4.659	**5**, 3297-3299 (2003)	38
		10, 4393-4396 (2008)	0
Organic Biomol. Chem.		**6**, 417-423 (2008)	6
Polym. Adv. Tech.	1.406	**16**, 189-194 (2005)	10
		18, 940-945 (2007)	6

		19, 596-601 (2008)	0
Polymer	2.773	**39**, 4505-4509 (1998)	14
		46, 8440-8447 (2005)	27
		49, 1761-1769 (2008)	3
Polymer Intl.		**57**, 6-10 (2008)	8
Proc. Natl. Acad. Sci., USA		**99**, 5110-5114 (2002)	128
		105, 20595-20600 (2008)	1
Soft Matter	4.391	**1**, 253-258 (2005)	16
		2, 886-891 (2006)	3
		3, 763-767 (2007)	1
		5, 1378-1385 (2009)	0
Tetrahedron Letters	2.509	**34**, 25, 3975-3977 (1993)	6
		48, 6839-6844 (2007)	3
Trans. Soc. For Biomater.		**22**, 229-231 (1999)	

Patents: (^ indicates licensed by a company)

1. Inventors: Russell, Thomas P., Tew, Gregory N., AL-Badri, Z., Shunmugam, R.
   Title: Ferromagnetic Materials via Direct Assembly of Block Copolymers: Design and Uses Thereof
   U.S. Patent Number: UMA 08-07, USSN 60/695,803

2. ^Inventors: DeGrado, William F., Tew, Gregory N., Klein, Michael L., Liu, Dahui, Yuan, Jing
   Title: Facially Amphiphilic Polymers as Anti-Infective Agents
   U.S. Patent Number: UMA 06-28, 7,173,102 PCT/US02/22043

3. ^Inventors: DeGrado, William F., Tew, Gregory, Arnt, Lachelle S.
   Title: Facially amphiphilic polymers and oligomers thereof, and use thereof in methods of treating cancer
   U.S. Patent Application: 20060241052 PCT/Pending

4. ^Inventors: Tew, Gregory, Ilker, M. Firat, Coughlin, E. Bryan
   Title: Amphiphilic polynorbornene derivatives and methods of using the same
   U.S. Patent Application: 20060115448 PCT/Pending

5. ^Inventors: DeGrado, William F., Tew, Gregory N., Klein, Michael L., Liu, Dahui, Yuan, Jing

Title: Facially amphiphilic polymers and oligomers and uses thereof
U.S. Patent Application: 20060041023 PCT/Pending

6. Inventors: Tew, Gregory, Bhatia, Surita
Title: Poly(lactic acid) copolymer hydrogels and related methods of drug delivery
U.S. Patent Application: 20060018872 PCT/Pending

7. ^Inventors: DeGrado, William F., Liu, Dahui, Tew, Gregory N., Klein, Michael L.
Title: Facially amphiphilic polyaryl and polyarylalkynyl polymers and oligomers and uses thereof
U.S. Patent Application: 20060115448 PCT/Pending

8. ^Inventors: DeGrado, William F., Tew, Gregory, Klein, Michael L.
Title: Facially amphiphilic polymers as anti-infective agents
U.S. Patent Application: 20040202639 PCT/US02/06899

Book Chapters:

1. S. I. Stupp, M. U. Pralle, P. V. Braun, G. N. Tew, P. Osenar, L. S. Li: Controlling Morphology through Self Assembling Supramolecular Materials: A Synthetic Route to Quantum Dots, Proc. of the 4th Inter. Symp. on Quantum Confinement: Nanoscale Materials, Devices, and Systems, Electrochem. Soc., M. Cahay, ed., 11, 3 (1997).
2. G. N. Tew, S. I. Stupp: Multifunctional Supramolecular Materials in *Functional Polymers: Modern Synthetic Methods and Novel Structures*, ACS Symp. Ser., A. O. Patil, D. N. Schulz, and B. Novak, Eds., 218 (1998).
3. S. I. Stupp, G. N. Tew, C. M. Whitaker: Programming Molecules to Form Supramolecular Materials in *Hyper-Structured Molecules I: Chemistry, Physics and Applications*, Gordon and Breach, H. Sasabe, ed. invited contribution, 9 (1999).
4.

At UMass-Amherst

5. * S. K. Agrawal, N. Sanabria-DeLong, K. Aamer, H. A. Sardina, S. R. Bhatia, G. N. Tew, Triblock PLLA-PEO-PLLA Hydrogels: Structure and Mechanical Properties, in *Polymeric Drug Delivery II: Polymeric Matrices and Drug Particle Engineering*, S. Svenson, Ed. ACS Symp. Ser., 102-119, (2006).
6. * G. N. Tew, K. Aamer, R. Shunmugam, Novel Block Copolymers with Terpyridine Pendant Groups, in *Metal-Containing and Metallo-Supramolecular Polymers and Materials*, G.R. Newkome, I. Manners, U.S. Schubert, Eds. ACS Symp. Ser., 126-140, (2006).
7. * K. Aamer, R. Shunmugam, G. N. Tew, Supramolecular Block Copolymers Containing Metal-Ligand Binding Sites: From Synthesis to Properties, in *Block Copolymer in Nanoscience*, M. Lazzari, S. Lecommandoux, and G. Liu, Eds. Wiley-VCH, 169-189, (2006).
8. * M. M. Slutsky, R. A. Blatchly, G. N. Tew, Foldamers: Nanoscale Shape Control at the Interface between Small Molecules and High Polymers, in *Physical Properties of Polymers Handbook*, J. E. Marks, Ed. Springer, 695-710, (2006).

9. * M. Firat Ilker, G. N. Tew, E. Bryan Coughlin, Amphiphilic Polymers with Potent Antibacterial Activity, in *Polymers and Materials for Anti-Terrorism and Homeland Defense*, J. G. Reynolds and G. Lawson, Eds. ACS Symp. Ser., in press, (2006).
10. * N. Sanabria-DeLong, K. A. Aamer, S. K. Agrawal, S. R. Bhatia, G. N. Tew: PLA-PEO-PLA Triblock Copolymers: Synthesis and Thermal Properties, in *Degradable Polymers and Materials – Principles and Practice*, K. Khemani and C. Scholz, Eds. ACS Symp. Ser., in press, (2006).

Published Meeting Abstracts:

The Polymer Chemistry and Polymer Materials: Science and Engineering Divisions of the American Chemical Society publish two-page extended abstracts for all invited, or contributed oral and poster presentations at the Spring and Fall National Meetings of the Society. These "pre-prints" are *not* peer reviewed prior to publication; however they are intended to serve as a pre-publication notice of work that typically will appear in the literature in the next six to twelve months. The authors, titles, and keywords of these pre-prints are listed in most major scientific database archives; however **no** citation record is kept by ISI for meeting abstracts. The pre-prints are very important to the industrial members of the Divisions. In addition, the pre-prints, which are required in order to present at the ACS meeting in these two Divisions, document participation. *A listing of "Non-Refereed Journals and Proceedings" is available at the end of this document.*

Media Coverage:

1. "Surfaces Designed to Kill Bacteria," by Stu Borman, *Chemical & Engineering News*, **80**, June 10, 2002.
   Describes our work on designing biomimetic antimicrobial polymers.
2. "Leading the Life Sciences, Growing the Commonwealth," Executive Breakfast hosted by University President William M. Bulger, Burlington, MA, October 30, 2002.
   Featured our work during the scientific presentation of highlights from the UMass-Amherst campus.
3. "Chemistry Highlights 2002," by Stu Borman, *Chemical and Engineering News*, **80**, December 16, 2002.
   This year-end recap highlighted our antimicrobial work.
4. "Gregory Tew Awarded Five Year Grant," *Rome Observer*, June 3, 2004.
   Announces me as one of 57 recipients nationwide of a $500,000 Presidential Early Career Award for Scientists and Engineers.
5. "Money Matters," *Hampshire Gazette*, June 23, 2003.
   Announces me as one of 26 professors honored as ONR Young Investigators from 220 applicants nationwide.
6. "Researchers," *MRS Bulletin*, July 2004.
   Announces me as one of 57 recipients nationwide of a $500,000 Presidential Early Career Award for Scientists and Engineers.
7. "Polymer Potential," *UMass Amherst Magazine*, Fall 2004.
   Mentions our receiving the $500,000 Presidential Early Career Award.
8. "Shedding New Light on Polymer Lanthanide Complexes," *Materials Today*, Nov 2004.
   Highlights the results from our *JACS* paper on lanthanide alloys.

9. "Research Highlights," *Nature*, Feb 2006.
   Highlights the results from our *JACS* paper on antimicrobial peptides.
10. "Why You Should Love Polymers," *UMass Amherst Magazine*, Winter 2006
   Mentions our work on antibacterial polymers.
11. "Putting Some Backbone into Bacterial Killers," *RSC Chemistry World*, Apr 2006.
   Highlights our work on antibacterial foldamers.
12. "Researchers Design Antimicrobial, Technique to Watch It," *Newswise*, Apr 2006.
   Highlights the results from our *Chem. & Biol.* paper on biomimetic facially amphiphilic antibacterial oligomers.
13. "Scientist' New Compound Defeats Drug-Resistant Bacteria," *In the Loop*, Jan 2009.
   Highlights a new synthetic compound that kills drug-resistant bacteria.
14. "UMass Scientist Taking Bacteria Down," *The Massachusetts Daily Collegian*, Jan 2009.

LIST OF PRESENTATIONS

-Presentation Statistics-

1. Invited Research Talks (since 2002) – 96
2. Contributed Research Talks – 56

Invited Lectures: (since 2002)

2002

"Antimicrobial Polymers," Army Natick Research Laboratories, Natick, MA, Feb, 2002.

"Polymers for Biology," Center for Tissue Engineering, University of Massachusetts-Medical School, Mar 2002

"Designing Facially Amphiphilic Antimicrobials," AIChE, Indianapolis, IN, Sept 2002

"Simple Facially Amphiphilic Polymers as Peptide Mimics," American Chemical Society, Boston, MA, Aug 2002

"Simple Facially Amphiphilic Polymers as Peptide Mimics," Solutia, Inc. Pensacola, FL, Sep. 2002

"Antimicrobial and Supramolecular Polymers," Army Research Laboratories, Aberdeen, MD, June 2002

2003

"Degradable Polymers and Antimicrobials," U of Minnesota, Minneapolis, MN, May 2003

"Proteomics to Antimicrobials," Bioengineering Research Partnership-NIH, Bethesda, MD. June 2003

"Designing Facially Amphiphilic Phenylene Ethynylenes," American Chemical Society, New York, NY, Sep 2003

"Biomimetic Polymers," Polymer for Advanced Technologies, Ft. Lauderdale, FL, Sep 2003

"Designing Antimicrobial Oligomers," University of Tennessee-Knoxville, Knoxville, TN, Nov 2003

"Antimicrobial Oligomers," Army Research Laboratories, Aberdeen, MD, Nov 2003

"Novel Antimicrobial Agents," Regional Technology Alliance, Holyoke, MA, Nov 2003

"Antimicrobial Oligomers for Antifouling Materials," Office of Naval Research Workshop, Orlando, FL, Dec 2003

"Facially Amphiphilic Polymers as Antimicrobials," Materials Research Society, Boston, MA, Dec 2003

2004

"Block Copolymers Containing Metal Ligand Side Chains for Use in Supramolecular Chemistry," American Chemical Society, Anaheim, CA, Mar 2004

"Facially Amphiphilic Phenylene Ethynylenes with Potent Antimicrobial Activity," American Chemical Society, Anaheim, CA, Mar 2004

"Bio-Inspired Materials," Becton-Dickinson, Franklin Lakes, NJ, May 2004

"Antimicrobial Polymers for Antifouling Materials," Office of Naval Research Workshop, San Francisco, CA, Jun 2004

"Chemically Rich Macromolecules," Laboratoire de Recherche Sur Les Polymères, Paris, France, July 2004

"Biomimetics to Supramolecular Polymers," Ecole Polytechnique Federale de Lausanne, Lausanne, Switzerland, July 2004

"Antimicrobial Polymers and Oligomers," GKSS Forschungszentrum, Geesthecht, Germany, July 2004

"Chemically Rich Macromolecules: Biomimetics to Supramolecular Materials," Eindhoven University of Technology, Eindhoven, The Netherlands, July 2004

"Proteomics to Antimicrobials," NIH, Bethesda, MD. July 2004

"Novel Antimicrobial Biomimetics," American Chemical Society, Philadelphia, PA, Aug 2004. Presentation as part of a Presidential Session

"Chemically Rich Macromolecules: Biomimetics to Supramolecular Materials," UMass-Lowell, Lowell, MA, Sep 2004

"Biomimetic Polymers," American Chemical Society Biennial, Savannah, GA, Oct 2004

"Merging Chemistry, Materials Science, and Biology to Create New Biomedical Materials," BEACON, Hartford, CN, Oct 2004

"Phenylene Ethynylene as a Versatile Biomimetic Backbone," Northeast Regional American Chemical Society Meeting, Rochester, NY, Nov 2004.

"Designing Antimicrobial Polymers," University of Mississippi, University, MS Dec 2004

2005

"Antimicrobial Biomimetics," Office of Naval Research Workshop, Sedona, AZ, Jan 2005

"Antimicrobial Polymers and Surfaces," PolyMedix Board Meeting, Radnor, PA, Feb 2005

"Chemically Rich Macromolecules: Biomimetic Antimicrobials and Metal Functionalized Copolymers," Northwestern University, Evanston, IL, Mar 2005

"Biomimetics Based on Phenylene Ethynylene Structures," American Chemical Society, San Diego, CA, Mar 2005

"Novel Hydrogels for Degradable Polymers," American Chemical Society, San Diego, CA, Mar 2005

"Chemically Rich Macromolecules," North Dakota State University, Fargo, ND, Apr 2005

"Macromolecules for Supramolecular Polymer Science Containing Metal-Ligands in the Side Chains," Northeast Regional American Chemical Society Meeting, Newark, NJ, May 2005.

"Antimicrobial Materials," Army Research Labs, Aberdeen, MD, May 2005

"Bioinspiried Macromolecules," Materials at the Synthetic Biological Interface-MRSEC, Amherst, MA, May 2005

"Chemically Rich Macromolecules," Virginia Tech, Blacksburg, VA, June 2005

"Non-Fouling Biomimetics," Office of Naval Research Workshop, Baltimore, MD, June 2005

"Phenylene Ethynylene Structures as Versatile Biomimetics," I.E.C.B., Bordeaux, France, June 2005

"Antimicrobial Polymers and Films," Gordon Research Conference, New London, NH, July 2005

"Capturing the Activity of Natural Proteins in Simple Polymers," The Society of Polymer Science Japan, Fukuoka, Japan, July 2005

"Design Molecules with Increased Functionality," Kyushu University, Fukuoka, Japan, July 2005

"Antimicrobial Oligomers and Polymers," N.I.H., Bethesda, MD, Aug 2005

"Antimicrobial and Metal-Ligand Polymers," University of Connecticut, Storrs, CT, Sept 2005

"Designing Macromolecules with Increased Functionality," North Carolina State University, Raleigh, NC, Nov 2005

"Designing Macromolecules with Increased Functionality: Strong Similarities to Biology," University of North Carolina, Chapel Hill, NC, Nov 2005

"Designing Macromolecules with Increased Functionality: Strong Similarities to Biology," Massachusetts Institute of Technology, Cambridge, MA, Nov 2005

"Biomimetic Materials Design," University of Michigan, Ann Arbor, MI, Nov 2005

"Designing Macromolecules with Strong Similarities to Biology," Kyoto University, Kyoto, Japan, Dec 2005

"Antimicrobial Polymers and Supramolecular Materials," Hokkaido University, Sapporo, Japan, Dec 2005

"Designing Macromolecules with Strong Similarities to Biology," Tokyo University, Tokyo, Japan, Dec 2005

"Tethered Biocides," ONR Workshop, Maui, HI, Dec 2005

"Metal Ligand Polymers for Supramolecular Materials," Pacifichem 2005 Congress Conference, Honolulu, HI, Dec 2005

2006

"Metal Containing Polymers for Self Healing Applications," Self-Healing Materials Workshop, Chapel Hill, NC, Jan 2006

"Designing Macromolecules with Strong Similarities to Biology," University of Illinois, Urbana, IL, Feb 2006

"Designing Macromolecules with Strong Similarities to Biology," Carnegie Mellon University, Pittsburgh, PA, Feb 2006

"Designing Macromolecules with Strong Similarities to Biology," University of Toronto, Toronto, Canada, Mar 2006.

"Capturing Host Defense Peptide Activity in Simple Oligomers," American Chemical Society, Atlanta, GA, Mar 2006

"Designing Macromolecules with Strong Similarities to Biology," Clemson University, Greenville, SC, April 2006

"Designing Macromolecules for NanoBiotechnology," PR-LSAMP, Mayagüez, Puerto Rico, May 2006

"Probing the molecular interactions of antimicrobial peptide mimics with SFG", American Chemical Society, San Francisco, CA, Sep 2006

"Designing Macromolecules with Strong Similarities to Biology," The Polytechnic University, New York, NY, Sep 2006

2007

"Designing Macromolecules with Strong Similarities to Biology," Polymer West, Gordon Research Conference, Ventura, CA, Jan 2007

"Designing Macromolecules with Strong Similarities to Biology," University of Alabama at Huntsville Chemistry Seminar Series, Jan 2007

"Designing Macromolecules with Strong Similarities to Biology," Polytechnic University, Brooklyn, NY, Feb 2007

"Metal-Containing Polymers," American Chemical Society National Meeting, Chicago, IL, Mar 2007

"Designing Antimicrobial Mimics for Host Defense Peptides," American Physical Society, Denver, CO, Mar 2007

"Nanotechnology at UMass-Amherst," INC3 Nanotechnology Conference on Communication and Cooperation, Brussels, Belgium, Apr 2007

"How to Obtain That First Tenure Track Faculty Position," NOBBChE Annual Conference, Los Angeles, CA, Apr 2007

"Designing Antimicrobial Mimics for Host Defense Peptides," Gordon Conference, Pisa, Italy, Apr-May 2007

"Designing Macromolecules with Strong Similarities to Biology," IUMACRO 2007, Polytechnic University, Brooklyn, NY, Jun 2007

"Designing Macromolecules with Strong Similarities to Biology," American Chemical Society Fall Meeting, Boston, MA, Aug 2007

"Designing Macromolecules with Strong Similarities to Biology," Biosensing Summer School, Larmor-Baden, France, Aug 2007

"Phenylene Ethynylene are Versatile Scaffolds for Bio-Nanotechnology," Iowa State University Chemistry Seminar Speaker, Sep 2007

"Designing Macromolecules with Strong Similarities to Biology," 9th International Symposium on Polymers for Advanced Technologies (PAT), Shanghai, China, Oct 2007

"Designing Macromolecules with Strong Similarities to Biology," STIPOMAT Conference, Les Diablerets, Switzerland, Oct 2007

"Designing Polymers with Strong Similarities to Biology" Rutgers University, New Jersey, Nov 2007

"Antimicrobial ROMP Polymers" ONR Coating Workshop, Sedona, AZ, Dec 2007

2008

"Designing Polymers Similar to Biology" NEA Partner Science Day, University of Puerto Rico, Mayaguez, Feb 2008 **Keynote Speaker*

"Designing Macromolecules with Strong Similarities to Biology" NOBCChE 35th National Conference, Phila, PA, Mar 2008

"Membrane-Active Synthetic Mimics of Host Defense Peptides" American Chemical Society Spring Meeting, New Orleans, LA, Apr 2008

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials" Macromolecular Chemistry Symposia, 101st National Meeting of the Korean Chemical Society, Seoul, Korea, Apr 2008

"Designing Macromolecules with Strong Similarities to Biology" MACRO 2008, Taipei, Taiwan, Jun-July 2008

"Designing Macromolecules with Strong Similarities to Biology," American Chemical Society Fall Meeting, Phila., PA, Aug 2008

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials," University of Florida-Gainsville, FL, Oct 2008

"Capturing Protein-like Activity in Synthetic Macromolecules," MACROMEX, Los Cabos, Mexico, Dec 2008

"Capturing Protein-like Activity in Synthetic Macromolecules," Eindhoven University, The Netherlands, Dec 2008

2009

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials," University of New Hampshire, Durham, NH, Feb 2009

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials," Global Center of Excellence, Kyushu University, Fukuoka, Japan, Apr 2009

"Landing Your First Tenure Track Faculty Position," NOBBChE 26th National Conference, St. Louis, MO, Apr 2009

"Novel Approaches to Non-Fouling Surfaces," Office of Naval Research Coatings Workshop, Portland, OR, Jun 2009

"Antimicrobial and Cell-Penetrating Peptide Mimics," 2009 Bioorganic Gordon Research Conference, Andover, NH, Jun 2009

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials," 2009 Polymers Gordon Research Conference, Mt. Holyoke College, Hadley, MA, Jun 2009

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials," University of Michigan, Sep 2009

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials," First Federation of Asian Polymer Societies (FAPS), Nagoya, Japan, Oct 2009

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials," Competence Centres for Excellent Technologies (COMET), Vienna, Austria, Oct 2009

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials," Cardinal Health, Dublin, OH, Oct 2009

"Chemically Rich Macromolecules: Biomimetics to Advanced Materials," 11th Annual Pacific Polymer Conference, Cairns, Australia, Dec 2009

2010

Upcoming

"Polymedix from Conceptualization of Synthetic Biopolymers to Commercialization," American Chemical Society Spring Meeting, San Francisco, CA Mar 2010

Contributed Talks: (since 2002)

2002

"Simple Facially Amphiphilic Polymers as Peptide Mimics," American Chemical Society, Boston, MA, Aug 2002

"Copolymers Containing Metal Binding Ligands for use in Supramolecular Materials: Toward Metal Induced Reversible Networks," American Chemical Society, Boston, MA, Aug 2002

"Phenylene Ethynylene Polymers with Amphiphilic Structures," American Chemical Society, Boston, MA, Aug 2002

2003

"Facially Amphiphilic Phenylene Ethynylenes at the Air-Water Interface," Polymers West Gordon Research Conference, Ventura, CA, Jan 2003

"Facially Amphiphilic Phenylene Ethynylenes," American Chemical Society, New Orleans, LA, Mar 2003

"Amphiphilic Secondary Structure in Phenylene Ethynylenes," American Chemical Society, New Orleans, LA, Mar 2003

"Aggregation Studies of Novel, Facially Amphiphilic Phenylene Ethynylenes," American Chemical Society, New Orleans, LA, Mar 2003

"Ortho Phenylene Ethynylene Molecules Programmed to form Secondary and Tertiary Structures," Polymers East Gordon Research Conference, South Hadley, MA, Jun 2003

"Aggregation Studies of Novel, Facially Amphiphilic Phenylene Ethynylene Materials," Polymers East Gordon Research Conference, South Hadley, MA, Jun 2003

"Synthesis of Terpyridine Containing Polymers with Well Defined Architectures for Use in Supramoleculars Materials," Polymers East Gordon Research Conference, South Hadley, MA, Jun 2003

"Triblock PLA-PEO-PLA Hydrogels: Structure and Mechanical Properties," American Chemical Society, New York, NY, Sep 2003

"Strong Gels from Associative PLA-PEO-PLA Triblock Copolymers," Society of Rheology, Pittsburgh, PA, Oct 2003

2004

"Optical and X-ray Scattering Studies on a Semi-crystalline Triblock Copolymer," American Physical Society, Montreal, Canada, Mar 2004

"Designing Novel Hydrogels for Applications in Biology," MRSEC-CAFP Joint Meeting, Amherst, MA, Jun 2004

"Macromolecules Containing Terpyridine in the Side Chain for Use in Supramolecular Materials," IUPAC, Jul 2004

"Triblock PLLA-PEO-PLLA Hydrogels: Structure and Mechanical Properties," IUPAC, Jul 2004

"Facially Amphiphilic Phenylene Ethynylenes: New Amphiphilic Architectures and Potent Antimicrobial Activity," IUPAC, Jul 2004

"Synthesis of Polyurea Oligomers and their Antibacterial Study," American Chemical Society, Philadelphia, PA, Aug 2004

"Cationic Facially Amphiphilic Phenylene Ethynylenes as Host Defense Peptide Mimics," American Chemical Society, Philadelphia, PA, Aug 2004

"PLA-PEO-PLA Hydrogels from Triblock Copolymers," American Chemical Society, Philadelphia, PA, Aug 2004

"Synthesis and Characterization of Substituted Ortho-phenylene Ethynylene Oligomers," American Chemical Society, Philadelphia, PA, Aug 2004

"Capturing Peptide Activity in Simple Oligomers: Access to New Markets and Opportunities," American Chemical Society, Philadelphia, PA, Aug 2004

"Synthesis and Characterization of Terpyridine-containing Polymer with Block-Random Architecture via Raft Polymerization," American Chemical Society, Philadelphia, PA, Aug 2004

"Macromolecules with Side Chain Terpyridine Motifs for Use in Supramolecular Materials," American Chemical Society, Philadelphia, PA, Aug 2004

"Cationic Facially Amphiphilic Phenylene Ethynylenes as Host Defense Peptide Mimics," Materials Research Society, Boston, MA, Dec 2004

"PLA-PEO-PLA Hydrogels," Materials Research Society, Boston, MA, Dec 2004

2005

"Chemically Rich Macromolecules: Antimicrobial Biomimetics and Self-Assembling Metal Functionalized Polymers," Polymers West Gordon Research Conference, Ventura, CA, Jan 2005

"Novel Antimicrobial Agents," American Society of Microbiology, Atlanta, GA, Apr 2005

"Influence of an Antibacterial Polymer on the Phase Behavior of Phospholipids," Biophysics of Membrane-Permeabilising and Membrane-Translocating Peptides Workshop, Berlin, Germany, Apr 2005

"Supramolecular Architectures Based on Metal Complexes," Polymers East Gordon Research Conference, South Hadley, MA, Jun 2005

"Controlling Mechanical properties of Hydrogels Through Crystalline Hydrophobic Domains," Gordon Research Conference, Polymers (East), South Hadley, MA, Jun 2005

"Folding of Ortho-Phenylene Ethynylene Oligomers Characterized by Solution NMR," Polymers East Gordon Research Conference, South Hadley, MA, Jun 2005

"Side Chain Terpyridine Polymers with Random and Blocky Architecture for Luminescence and 'Nano' Assembly Applications," Polymers East Gordon Research Conference, South Hadley, MA, Jun 2005

"Preventing Bacterial Colonization on Synthetic Polymer Surfaces," American Society of Microbiology, Hartford, CT, Jun 2005

"Antimicrobial Films and Coatings," Films and Coatings Gordon Research Conference, New London, NH, Jul 2005

"Synthesis and Characterization of Electronic Variations of Ortho-Phenylene Ethynylene Oligomers," American Chemical Society, Washington, DC, Aug 2005

"Tunable Hydrogels from PLA-PEO-PLA Triblocks: Effect of Crystallinity of the PLA Block," Society of Rheology, Vancouver, British Columbia, Oct 2005

"Using Crystallinity to Control Structure and Rheology of PLA-PEO-PLA Hydrogels," AIChE Materials Engineering and Sciences Division Annual Meeting, Cincinnati, OH, Oct 2005

"Metal-Ligand Polymers Containing Lanthanide Ions," Materials Research Society, Boston, MA, Dec 2005

"Designing Polymers to Capture the Biological Activity of Host Defense Peptides," Materials Research Society, Boston, MA, Dec 2005

"Antimicrobial Biomimetic Molecules," Pacifichem 2005 Congress Conference, Honolulu, HI, Dec 2005

2006

"Designing Macromolecules with Strong Similarities to Biology," ACS Spring National Meeting, Atlanta, GA, Mar 2006

"Influence of an Antibacterial Polymer on the Phase Behavior of Phospholipids," Small Angle Scattering Conference SAS2006, Kyoto, Japan, Jun 2006

"Designing Antimicrobial Polymers as Host Defense Mimics," IUPAC, Macro 2006 World Polymer Conference, Rio De Janeiro, Brazil, Aug 2006

"Supramolecular Assembly of Polymers Containing Metal Ligands in the Side Chain," IUPAC, Macro 2006 World Polymer Conference, Rio De Janeiro, Brazil, Aug 2006

"Blocky Macromolecules Containing Terpyridine for Supramolecular Materials," American Chemical Society, San Francisco, CA, Sep 2006

"Designing Polymers for Biological Activity," American Chemical Society, San Francisco, CA, Sep 2006

"Novel Antibiotics for the Emerging Problem of Drug Resistant Bacteria," American Chemical Society, San Francisco, CA, Sep 2006

2007

"Synthesis and Activity of Novel Antimicrobial Surfaces," American Chemical Society, Boston, MA, Aug 2007

"Influence of Lipid Composition on Membrane Activity of Antimicrobial Oligomers," American Chemical Society, Boston, MA, Aug 2007

"1H NMR Characterization of Helical Folding in *ortho*-Phenylene Ethynylene Oligomers," American Chemical Society, Boston, MA, Aug 2007

"Sensing Chemical Warfare Agents with Terpyridine-based Macromolecules," American Chemical Society, Boston, MA, Aug 2007

"Side Chain Terpyridine Motifs for Supramolecular Materials," American Chemical Society, Boston, MA, Aug 2007

"Amphiphilic Polymers Endowed with Desirable Antimicrobial Properties," American Chemical Society, Boston, MA, Aug 2007

"Nanomagnetic Polymers," American Chemical Society, Boston, MA, Aug 2007

"Directed Self-Assembly of Polymers and Nanotubes into Air-Suspended Bridges," 13th Annual Kentucky EPSCOR Conference, Lexington, KY, Oct 2007

RESEARCH FUNDING

Raised $13,938,720 since starting at UMass in September 2001. Funding from federal agencies include NSF, NIH, ARO, and ONR. This does not include my efforts on major center and equipment grants; it only includes research dollars directly into my laboratory.
**indicates I am PI, where I am not PI only funds under my control are listed*
#direct cost only

Current

NIH U01 (PI: Tew) – "Antimicrobial Oligomers for BioDefense and Emerging Food-borne Infectious Disease" $8,681,382 (06/09-05/14)

NSF CAREER Award* - "Programming Molecules to Fold into Helical Structures" $515,000# (1/05-12/09)

NIH:UPENN (PI: Wm. DeGrado) – "Antibacterial Foldamers" $500,000 (4/08-3/12)

ONR* - "Natural Immunity Approaches to Anti-Fouling Coatings" $464,722 (01/07-9/09)

ARO (PI: Tew) – "Ferromagnetic Materials by Directed Self-Assembly of Novel Polymers" $450,000 (09/09-08/12)

NSF/NIRT: University of Louisville (PI: Bob Cohen) - "Directed Self-Assembly of Suspended Polymer Fibers in the Fabrication of 3-D Nanodevices" $345,981 (9/05-8/09)

NSF (PI: Maria Santore) – "Surfaces that Selectively Manipulate and Kill Bacteria" $225,000 (09/08-08/11)

CUMIRP Part I: Cluster B – "Novel Hydrogels" $27,000, 10/08-09/09

NSEC: CHM (PI-Jim Watkins) – "Novel Water-based Assemblies" $15,000# (03/08-03/09)

ARO* DURIP $150,000 (equipment grant)

NSEC: CHM-JUNTO (PI: Jim Watkins) "Hydrogel Characterization" $23,250# (11/08-10/09)

MRSEC– NSF funded (PI-Tom Russell) - "Amphiphilic Block Copolymers" $25,000# (05/09-04/10)

GATES FOUNDATION (PI: Tew) "Capturing Nature's Weapons to Prevent Infectious Disease" $100,000 (5/1/09-04/30/10)

Pending

Army Medical Research (PI: Tew) – "Antimicrobial Oligomers-Harnessing Nature's Immunity for Wound Healing" $859,293 (09/09-08/14)

NIH (PI: Tew) – "Corneal Tissue Engineering: Designer Synthetic Networks to Reinforce Recombinant Collagen Scaffolds" $1,839,919 (06/09-05/14)

NSF (PI: Tew) – "Guanidine Rich Synthetic Macromolecules: Transduction Domain Mimics" $581,647 (06/09-05/12)

NSF: Polymedix (R. Scott) – "Antimicrobial Sutures" $40,000 (1/1/10-06/30/10)

ONR: Polymedix (R. Scott) – "STTR for N09-T033: Novel IV Antibiotic for Acinetobacter Infections" $35,600 (10/1/09-09/30/10)

ARO: Polymedix (R. Scott) – "STTR for A09A-T004: Novel Antibiotics for MDR Biofilm Injections" $35,600 (10/1/09-9/30/10)

Army Research Office (ARO) (PI: Tew) – "Novel Polymers Containing Metal Ligands in the Side Chain" $300,000 (9/1/09-8/31/12)

Completed

ARO Young Investigator* Presidential Early Career Award for Scientists and Engineers - "Supramolecular Materials from Metal Functionalized Copolymers" $500,000 (6/04-5/09)

ARO-MURI (PI-Russell) - "Bio-Directed Hierarchical Assembly of Multifunctional Materials" $300,000 (6/04-5/09)

MRSEC– NSF funded (PI-Tom Russell) - "ABC Triblock Copolymers" $27,000# (05/08-04/09)

PolyMedix Sponsored Research* - "Facially Amphiphilic Polymers for Self-Sterilizing Materials" $325,660 (10/03-08/08)

CUMIRP Part III: Bausch & Lomb" $7,000 (01/07-01/08)

DuPont Young Faculty Grant* $75,000 (11/04-10/07)

NIH (PI-Bill DeGrado) - "Proteomics to Biomimetic Polymers: Engineering Principles for Anti-Infective Agents" $411,785 (9/02-9/07)

ONR* - "Bioactive Surfaces" symposia support $4,000 (8/05-12/06)

ONR Young Investigator* - "Biomimetic Approaches to New Antifouling Materials" $380,000 (5/03-5/06)

CUMIRP- Cluster B-Polymers in the BioArena* - "Biodegradable Hydrogels" $90,000 (9/03-8/06)

Army Research Laboratory Center of Excellence on Polymers (PI-Sam Gido) – "Polymers for Supramolecular Materials" $71,588 (1/04-12/05)

NSF-IMR (PI- Thayumanavan) - "Acquisition of a Gel Permeation Chromatography with Multiple Detection System for Polymer Research and Education" $76,001 (1/04-12/05)

3M Nontenured Faculty Award* $45,000 (7/02-7/05)

Army Research Office DURIP* - "Macromolecular Sample Characterization" $99,966 (1/03-6/05)

MRSEC– NSF funded (PI-Tom Russell) - "Metal Ligand Containing Polymers" $75,000# (5/02-5/05)

NSF Research Site for Educators in Chemistry (PI-Tom McCarthy) - "Computational Prediction of Helical *ortho* Phenylene Vinylenes" $69,750 (5/02-5/05)

Army Research Laboratory Directors Research Initiative* - "Decontaminating Polyurethanes" $35,000 (1/04-12/04)

Army Research Laboratory - Center of Excellence on Polymers (PI-Sam Gido) – "Polymers for Supramolecular Materials" $28,635 (1/03-12/03)

University of Massachusetts Faculty Research Grant*- "Facially Amphiphilic Polymers" $15,000 (2/02-2/03)

Army Research Office Short Term Innovative Research* - "Biomimetic Polymers with Antimicrobial Activity" $30,000 (7/02-1/03)

Total: $13,938,720 (not including pending)

TEACHING RECORD

Course No.	Course Title	Credits	Enrollment	Course Evaluation (out of 7)

2001-02 Academic Year				
-Fall Term-				
	No teaching assignment			
-Spring Term-				
PSE 760	Organic Polymerization Reactions	3	23	5.78
Chem 496	Undergraduate Lab Research	1	1	n/a
2002-03 Academic Year				
-Fall Term-				
PSE 603	Polymer Synthesis Laboratory	3	20	5.62
Chem 496	Undergraduate Lab Research	6	2	n/a
-Spring Term-				
PSE 760	Organic Polymerization Reactions	3	16	5.63
Chem 496	Undergraduate Lab Research	6	2	n/a
Chem 388	Undergraduate Research	3	1	n/a
2003-04 Academic Year				
-Fall Term-				
PSE 603	Polymer Synthesis Laboratory	3	22	5.55
Chem 496	Undergraduate Lab Research	6	6	n/a
-Spring Term-				
PSE 760	Organic Polymerization Reactions	3	21	5.01
2004-05 Academic Year				
-Fall Term-				
PSE 603	Polymer Synthesis Laboratory	3	22	5.88
Chem 496	Undergraduate Lab Research	6	3	n/a
MicBio 396 H	Microbiology Honors Independent Study		1	
MicBio 696	Microbiology Independent Study		1	
MicBio 796	Microbiology Independent Study		1	
-Spring Term-				
PSE 760	Organic Polymerization Reactions	3	21	5.55
2005-06 Academic Year				
-Fall Term-				

PSE 607	Introduction to Polymer Chemistry	3	26	4.99
Chem 496	Undergraduate Lab Research	3	5	n/a
BioChem 396H	Biochemistry Honors Independent Study		2	5.23
-Spring Term-				
PSE 760	Organic Polymerization Reactions	3	18	5.23
PSE 797D	Scientific & Engineering Management	1	26	4.53
PSE 897T	Well-Defined Macromolecular Arch.	1-3	6	
Chem 499T	Chemistry Honors Thesis		1	
MicBio 396H	Microbiology Honors Independent Study		1	
2006-07 Academic Year				
-Fall Term-				
PSE 607	Introduction to Polymer Chemistry	3	26	4.20
PSE 897T	Well-Defined Macromolecular Arch.	1-3	4	
-Spring Term-				
PSE 760	Organic Polymerization Reactions	3	23	
PSE 797D	Scientific & Engineering Management	1	9	
PSE 897T	Well-Defined Macromolecular Arch.	1-3	6	
2007-08 Academic Year				
-Fall Term-				
PSE 607	Introduction to Polymer Chemistry	3	29	
PSE 897T	Well-Defined Macromolecular Arch.	1-3	5	
BioChem 296H	Biochemistry Honors Independent Study		3	
-Spring Term-				
PSE 797D	Scientific & Engineering Management	1	1	
PSE 897T	Well-Defined Macromolecular Arch.	1-3	9	
2008-09 Academic Year				
-Fall Term-				

PSE 603	Polymer Synthesis Lab	3	30	
PSE 897T	Well-Defined Macromolecular Arch.	1-3	6	
-Spring Term-				
PSE 760	Organic Polymerization Reactions	3	24	
PSE 797D	Scientific & Engineering Management	1	7	
PSE 897T	Well-Defined Macromolecular Arch.	1-3	9	

Student Thesis Committees

Student	*Department*	*Thesis Type*	*Status*
Semra Colak	Polymer Science	PhD	Current
Jeremy Rathfon	Polymer Science	PhD	Current
Adam Hathorne	Polymer Science	PhD	Current
Naomi Sanabria-DeLong	Polymer Science	PhD	Graduated
Sterling Alfred	Polymer Science	PhD	Graduated
Joanna Pool	Polymer Science	PhD	Graduated
Khaled Aamer	Polymer Science	PhD	Graduated
Ticora Jones	Polymer Science	PhD	Graduated
Firat Ilker	Polymer Science	PhD	Graduated
Lachelle Arnt	Polymer Science	PhD	Graduated
Roberto Laos	Polymer Science	PhD	Graduated
Sungkyun Sohn	Polymer Science	PhD	Graduated
Jason Rennie	Microbiology	MS	Graduated
Kyoung-sik Chin	Chemical Eng	PhD	Graduated
Praveen Sharma	Chemical Eng	PhD	Graduated
Chandrakant Popere	Chemistry	PhD	Current
Chae Kyu Kim	Chemistry	PhD	Current
Adrienne Carver	Chemistry	PhD	Current
Dipankar Basak	Chemistry	PhD	Current
Basar Gider	Chemistry	PhD	Graduated
Arlicia Grant	Chemistry	PhD	Graduated
Hao Xu	Chemistry	PhD	Graduated
Hiroshi Nakade	Chemistry	PhD	Graduated
Jitapa Sumranjit	Chemistry	PhD	Graduated
Kulandaivelu Sivanandan	Chemistry	PhD	Graduated
Jeff Martin	Chemistry	PhD	Graduated
Patrick Taylor	Chemistry	PhD	Graduated
Travis Benanti	Chemistry	PhD	Graduated
Safo Abaoku	Chemistry	PhD	Graduated
Kyrs Bronk	Chemistry	PhD	Graduated
Sarah Lyon	Chemistry	Undergraduate Honors	Graduated
Courtney McConoghy	Chemistry	Undergraduate Honors	Graduated
Katelyn Spillane	Chemistry	Undergraduate Honors	Graduated

Eric Turnberg	Chemistry	Undergraduate Honors	Graduated
Tatyana Shalapyonok	Chemistry	Undergraduate Honors	Graduated
Jeff Dabkowski	Microbiology	Undergraduate Honors	Graduated
Chris Nelson	Microbiology	Undergraduate Honors	Graduated

SERVICE CONTRIBUTIONS

To the University:

1. Faculty Participant, Materials Research Science and Engineering Center (MRSEC), 2001-present. The center coordinates collaborative polymer research efforts on campus under a multi-investigator NSF grant. Reviews are held on-campus twice annually as part of the renewal process. For the 2001-02 renewal, I was a major contributor to writing the final proposal as part of IRG III. This new IRG effort increased the MRSEC funding by 33% from past years. My role in outreach and diversity has increased as the Center's focus on this area has expanded.
2. Faculty Participant, Center for UMass-Industry Research on Polymers (CUMIRP), 2001-present. This center organizes polymer research between the university and industrial partners. Two on-campus reviews are held annually. I actively participated in the planning and formation of a new cluster (Cluster B- Polymers in the BioArena) which currently has three members that are entirely new to CUMIRP. These include Johnson & Johnson and Boston Scientific. Attracting new CUMIRP members is essential to expanding the financial base of this center as opposed to past trends in which new clusters were formed by moving companies from old clusters. I co-organized the 2002-2003 CUMIRP workshop, "Polymer Biomaterials" and the 2003 Fall poster session.
3. Executive Committee Member, Chemistry-Biology Interfaces Program (CBI), member since 2001, Executive Committee since 2003-present. This is a campus-wide NIH funded program to train students in the interdisciplinary interface of chemistry and biology. The program meets monthly with presentations by the active faculty and their students.
4. Recruiting Committee Chairman, Chemistry-Biology Interfaces Program (CBI) since 2003-2006. This committee is charge with recruiting responsibilities for the program including minority recruiting. Because this is a non-degree program, recruiting spills over into departmental efforts. There are representatives from Chemistry, Chemical Engineering, Polymer Science and Engineering, and Biochemistry. As chairman, I helped integrate this effort with the larger campus-wide NEAGEP.
5. Recruiting Committee Member, Chemistry-Biology Interfaces Program (CBI) since 2006-present.
6. Participant, Lunch Panel, "A Ph.D. is not Enough." This is a student-initiated effort to increase mentorship within the graduate student body on the UMass campus. It is generally in-line with a larger goal and, now, campus-wide mission to increase mentorship activities on Campus.
7. Member, Equal Access to the Sciences for All Genders and Ethnicities (EASAGE) committee since 2004-present. This is a College-wide committee to address greater diversity access in the physical sciences.
8. Faculty Mentor, NEAGEP, 2004-present.

9. Recruiting, Science, Engineering, and Health Professions Collaborative Symposium, January 19, 2006, University of Connecticut. A diversity event.
10. Speaker, IGERT presentation for PSE course 590A, "Nanotechnology from Lab to Product" to discuss translating research into technology.
11. Member, Stockroom Bid Committee, 2003. Our responsibility was to evaluate competing bids for the chemical stock room located in the basement of LGRT. This also included gathering feedback from my department on the need and use of this facility. We, the committee, proposed a recommendation and supervised the implementation of this recommendation. The stockroom was converted from VWR to Fischer and most patrons have expressed pleasure with the new stockroom.
12. Co-organized the 2002 Lenz symposium held at the Campus Center. Although this meeting was held to recognize a retired PSE faculty member, the committee raised money and organized an international symposium held on campus which highlighted the UMass scientific community.
13. I participated in the campus effort to establish the Security, Emergency Preparedness, and Response Institute (SEPRI), which assembles talent campus-wide to address current challenges in homeland defense. I was involved in the initial planning meetings with Vice Chancellor Fred Byron and presented at the kick-off meeting held on April 29-30, 2003.
14. My involvement with PolyMedix led to a term sheet with the University in which PolyMedix expects to contribute 1 million in research dollars to my lab over the next five years (as of January 2006 this total is $356,140). In addition, the University gains a 3% ownership in PolyMedix. This activity nicely illustrates the integrated scientific and technological aspects of my research and how they can benefit the University in multiple ways.
15. Active participant in the NEAGAP program on campus. This involves the targeted recruiting and development of minority science students for careers in academia. Other activities include screening, hosting, and interacting with undergraduates as part of the SPUR program run by NEA. My participation has built and strengthened PSE's recruiting and retention mission with the larger University effort on diversity. Attended the National Organization for the Professional Advancement of Black Chemists and Chemical Engineers (NOBCChE) national annual meeting 2004, 2005, 2006, 2009.
16. Annual reviewer of abstracts for the Commonwealth Undergraduate Research Conference. This past year was the 10th annual and my second term as a reviewer (2003-04).
17. Co-organizer, American Chemical Society Polymer Division 6th National Graduate Student Research Conference. (also listed under Departmental service). Because this conference attracted national and international attention, it is listed as University service.

To the Polymer Science and Engineering Department:

1. Member, Departmental Awards Committee since 2002-present. This committee responsible for identifying, nominating, and pursuing awards for PSE faculty.
2. Member, Space and Facilities Committee since 2002-present. This committee is responsible for overseeing and allocating research and office space within the Conte building.

3. Member, Polymer Synthesis Curriculum Committee since 2003-present. This committee is responsible for updating and evaluating the synthetic polymer chemistry component of the department's graduate studies.
4. Member, Recruiting Committee since 2003-present. This committee is responsible for increasing the number and quality of graduate students admitted each year. Our first departmental recruiting material was developed, which is an 11x18 poster with tear off cards with departmental information. We have also created a trifold, single sheet flyer for mass mailing distribution. We changed our recruiting strategy to include a weekend recruiting event for prospective 1st years. Another change included eliminating the 'interview' process for the highest quality prospective students.
5. New website, co-organizer of the effort to launch a new PSE website.
6. PSE Faculty's Publications Book. I developed and created a single volume book that included all of the PSE faculty publications for 2004 and 2005. This was well received. The 2006 edition is in the final stages of printing.
7. Member, 2004-2005 Faculty Search Committee.
8. Co-organizer, American Chemical Society Polymer Division 6th National Graduate Student Research Conference. This conference is focused on graduate student presentations. In addition, special sessions were organized on Career Development and mentoring. This conference had the largest attendance to date. In addition, we had international participation.
9. Member, Panel for Scientific Management Class, 2004 and 2005. Participated on this panel to discuss 'my path to a tenure track faculty position.'

To the Professional Community:

External Educational and Professional Activities:

1. Co-founder and Scientific Advisor Board member, Polymedix, Inc, Philadelphia, PA, 6/02-present.
2. Member, ACS Polymer Division board, 2002-current.
3. Alternate Councilor, ACS Polymer Division. 2005-current.
4. Program Committee, Polymers West Gordon Conference. 2006-2007.
5. Co-chair, Graduate Research Conference on Polymers, Gordon Conference, 2006-2007.
6. Member, Editorial Board, Polymers for Advanced Technologies, 2006-present.
7. Program Chair, ACS Polymer Division, 2009-2010.
8. Co-organizer, NOBCChE, April 2006. Workshop entitled "Landing Your First Tenure-Track Position." This workshop outlines the practical steps taken by recent young faculty to secure their positions.
9. Co-organizer, 2005 ACS Fall Meeting symposia entitled "Bioactive Surfaces and Their Applications."
10. Co-organizer, ACS Polymer Division 6th National Graduate Student Research Conference, June 2005.

11. Co-organizer, ACS Polymer Division 2004 Biennial, Oct 2004. This is the keynote meeting of the ACS Polymer Division. This symposium addresses current topics and aims to set the course for emerging and future areas of polymer research.
12. Session Chair, Polymers West Gordon Research Conference, 1/03. I was invited by the Conference Chair and co-Chair to moderate the morning session of presenters.
13. Chair, ACS National Fall Meeting, Biomacromolecules Session, 2002.
14. Secretary, Oak Ridge National Laboratory, Center for Nanoscale Materials Science Workshop, 2002
15. Volunteer, Encouraging Tomorrow's Chemists, Middle School Outreach, University of Illinois, Urbana, 8/96-12/98
16. Panelist, National Science Foundation Panel, VA, 08/08
17. Chair, ACS National Fall Meeting, Polymer Chemistry Session, 08/09

Reviews of Publications and Proposals:

Proposals

National Science Foundation (NSF) – Reviewer for the Divisions of Chemistry and Materials Research
1. Organic and Macromolecular Program
2. Polymer Program

NSF CAREER Panel
NSF Nanoscale Integration Research Team (NIRT)
Petroleum Research Fund
National Institutes of Health (NIH) special study section
Department of Energy, Center for Nanophase Materials Science, Proposal Review Committee

Journals

Listed in approximate order of frequency
Journal of the American Chemical Society
Angewandte Chemie
Macromolecules
Journal of Polymer Science-Polymer Chemistry-Part A
Biomacromolecules
Journal of Organic Chemistry
Organic Letters
Chemistry and Biology
Polymer
Chemistry: European Journal
Chemical Communications
Chemical Materials
Langmuir
Journal of Materials Chemistry
Journal of Physical Chemistry B
Biomaterials
Macromolecular Chemistry and Physics

Tetrahedron Letters
MRS Bulletin
Soft Matter
Journal of Controlled Release
Journal of Industrial Microbiology & Biotechnology
Advanced Functional Materials
Biochima et. Bio Physica. Acta
Microbiology-SGM
Molecular Crystals and Liquid Crystals
Polymers for Advanced Technologies

Consulting Activities:

Polymedix, Inc., Philadelphia, PA, 2002-present.
Pestaway Company, West Falmouth, MA, 2003-2004.

RESEARCH GROUP

Current Postdoctoral Research Fellows

Dr. Abhigyan Som
Dr. Jing Jiang
Dr. Ke Zhang

Current Graduate Students

Semra Colak –4th year
Raghavendra Maddikeri – 4th year
Arife Ozgul Terife – 3rd year
Jun Cui (with Al Crosby) – 3rd year
Hitesh Thaker – 3rd year
Yongping Zha – 3rd year
Melissa Lackey – 2nd year
Michael Lis – 2nd year
Catherine Walker – 1st year
Katherine Gibney – 1st year

Current Undergraduate Students

Joshua Grolman
Nidhi Kumar
Nikita Nayyar
Kewei Zhang
Avital Percher

Group Alumni:

Jeremy Rathfon	graduate (Ph.D.)	
Sterling Alfred	graduate (Ph.D.)	Post-doc, Duke University
Naomi Sanabria-DeLong	graduate (Ph.D.)	W. L. Gore & Associates
Khaled Aamer	graduate (Ph.D.)	NIST, Biomaterials Group
Ticora Jones	graduate (Ph.D.)	Sen. Russ Feingold's Office

Lachelle Arnt	graduate (Ph.D.)	Clorox, Inc.
Jason Phillip	graduate (MBA)	Arthur Lok Jack Graduate School of Business, University of the West Indies
Jason Rennie	graduate (M.S.)	UMass Worcester
Ahmad Madkour, Ph.D.	post-doc	Dow Chemical
Karen Lienkamp. Ph.D.	post-doc	Univ. of Freiburg, Germany
Raja Shunmugam, Ph.D.	post-doc	I.I.S.E.R., Kolkata, India
Morris Slutsky, Ph.D.	post-doc	B.R.C., UMass Dartmouth
Gregory Gabriel, Ph.D.	post-doc	Kennesaw State University
Zoha AL-Badri, Ph.D.	post-doc	Ashland-Hercules, Inc.
Haizhong Tang, Ph.D.	post-doc	PolyMedix, Inc.
Jeff Dabkowski	graduate (M.S.)	Northeastern University
Sarah Lyon	undergraduate	Massachusetts College of Pharmacy & Health Sciences
Chris Nelson	undergraduate	Massachusetts College of Pharmacy & Health Sciences
Katelyn Spillane	undergraduate	UC-Berkeley
Yelena Urgina	undergraduate	Westfield Electroplating Co.
Dannon Stigers	undergraduate	Univ. of New Hampshire
Jack Peters	undergraduate	Ion Corp
Tatyana Shalapyonok	undergraduate	N. E. School of Optometry
Katelyn Spillane	undergraduate	UC Berkeley
Debanti Sengupta*	undergraduate	Stanford

joint w/Patricia B. O'Hara, Amherst

Graduate Visiting Scholars

Amelie Koch	Ph.D. Candidate	Technical University of Munich, Germany
Federica Sgolastra	Ph.D. Candidate	Polytechnic University of Marche, Ancona, Italy

Undergraduate Summer Students (REU)

Aaron Zimmerman	Swarthmore College
Jordan Gruskay	Amherst College
Aleksandr Gerasimenko	Oregon State University
Louis Perez	University of Florida
Yamalia Roberts	University of Connecticut
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Cartney E. Smith	Brown University
Jesus Garcia	University of Puerto Rico, Mayaguez
Ashlan Musante	Wheaton College

Educator Summer Students (RET)

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Angela Cote	Ralph C. Mahar Regional High School
Paralee King, Chemistry	Quabbin Regional High School

Undergraduate Research Exchange Students

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Anika Reuters, University of Mainz, Germany
Henning Schafer, University of Mainz, Germany
Christoph Kins, University of Mainz, Germany
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Prof. Surita Bhatia, University of Masschusetts-Amherst
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Prof. Michael Klein, University of Pennsylvania
Prof. Ka-Yee Lee, University of Chicago
Prof. Klaus Nüsslein, University of Massachusetts-Amherst
Prof. Susan Roberts, University of Massachusetts-Amherst
Dr. Regine Willumeit, GSSK, Germany
Prof. Zhan Chen, University of Michigan
Prof. Gerard Wong, University of Illinois
Prof. Robert Cohn, University of Louisville
Prof. Robert Keynton, University of Louisville
Prof. Gareth McKinley, Massachusetts Institute of Technology
Prof. Ji-Young Chang, Seoul National University, Korea
Prof. Shen Ye, Hokkaido University, Japan

Non-Refereed Journals and Proceedings:

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8. * G. N. Tew, "Amphiphilic Phenylene Ethynylenes," *Polymer Preprints*, **44 (2)**, 452, (2003).
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